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FORM PTO-1390 (Modified) (REV 10-95) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		ATTORNEY'S DOCKET NUMBER 01123.0004 U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 09/509712
INTERNATIONAL APPLICATION NO. **PCT/US98/21276**	INTERNATIONAL FILING DATE **8 October 1998**	PRIORITY DATE CLAIMED **10 October 1997**

TITLE OF INVENTION

MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION

APPLICANT(S) FOR DO/EO/US

RUBIN, Donald H.; ORGAN, Edward L.; DUBOIS, Raymond N.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☒ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☐ A copy of the International Search Report (PCT/ISA/210).
8. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
9. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
10. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 13 to 18 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
    A **SECOND** or **SUBSEQUENT** preliminary amendment.
16. ☐ A substitute specification.
17. ☐ A change of power of attorney and/or address letter.
18. ☒ Certificate of Mailing by Express Mail
19. ☒ Other items or information:

Check in the amount of $943.00 for filing fees; return-receipt postcard; Certificate of Express Mailing No. EL348124625US; Verified Statements Claiming Small Entity Status signed by Vanderbilt University and by Avatar BioSci, Inc.

PCTUS1/REV03

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U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 09/509712	INTERNATIONAL APPLICATION NO. PCT/US98/21276	ATTORNEY'S DOCKET NUMBER 01123.0004

20. The following fees are submitted:.

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :

		CALCULATIONS	PTO USE ONLY
☒ Search Report has been prepared by the EPO or JPO	**$840.00**		
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482)	**$670.00**		
☐ No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2))	**$760.00**		
☐ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO	**$970.00**		
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)	**$96.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =		**$840.00**	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).		**$0.00**	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	29 - 20 =	9	x $18.00	**$162.00**	
Independent claims	11 - 3 =	8	x $78.00	**$624.00**	
Multiple Dependent Claims (**check if applicable**).			☒	**$260.00**	
	TOTAL OF ABOVE CALCULATIONS		=	**$1,886.00**	
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) (**check if applicable**).			☒	**$943.00**	
	SUBTOTAL		=	**$943.00**	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).			+	**$0.00**	
	TOTAL NATIONAL FEE		=	**$943.00**	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (**check if applicable**).			☐	**$0.00**	
	TOTAL FEES ENCLOSED		=	**$943.00**	
				Amount to be: refunded	$
				charged	$

☒ A check in the amount of **$943.00** to cover the above fees is enclosed.

☐ Please charge my Deposit Account No. in the amount of to cover the above fees. A duplicate copy of this sheet is enclosed.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **14-0629** A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Janice A. Kimpel, Ph.D.
NEEDLE & ROSENBERG, P.C.
127 Peachtree Street, N.E., Suite 1200
Atlanta, Georgia 30303 U.S.A.
(404) 688 0770

Janice A. Kimpel
SIGNATURE

Janice A. Kimpel
NAME

42,734
REGISTRATION NUMBER

March 30, 2000
DATE

09/509712
430 Rec'd PCT/PTO 31 MAR 2000

CERTIFICATE OF EXPRESS MAILING

I hereby certify that the filing of the U.S. National Phase in the names of Rubin *et al.*, consisting of: Transmittal Letter to the United States Designated/Elected Office (DO/EO/US) Concerning a Filing Under 35 U.S.C. 371 (2 pages), a check in the amount of $943.00 for filing fee, Verified Statement Claiming Small Entity Status by Vanderbilt University (2 pages), Verified Statement Claiming Small Entity Status by Avatar BioSci, Inc. (2 pages), Declaration/Power of Attorney by Rubin, Organ & Dubois and return-receipt postcard are being deposited with the United States Postal Service as Express Mail No. EL348124625US in an envelope addressed to: Box PCT, Assistant Commissioner for Patents, Washington, D.C., 20231, on this **30th** day of **March 2000.**

Everardo McFarlane

3-30-2000
Date

H:\apps\ss\docs\jak\W054171.WPD

Applicant or Patentee: Donald H. Rubin, Edward L. Organ and Raymond N. Dubois

For: **"MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION"**

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) and 1.27(d)) - SMALL BUSINESS CONCERN

I hereby declare that I am

[ ] the owner of the small business concern identified below:
[X] an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF CONCERN: Avatar Biosci, Inc.
ADDRESS OF CONCERN: 1937 Edenbridge Way
Nashville, TN 37215

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18(d), for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled **"MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION"** by inventor(s) Donald H. Rubin, Edward L. Organ and Raymond N. Dubois described in the specification filed concurrently herewith.

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

*NOTE: Separate verified statements are required for each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

NAME: VANDERBILT UNIVERSITY

ADDRESS: Office of Technology Transfer
1207 17th Ave. S., Suite 210
Nashville, TN 37212

[ ] INDIVIDUAL [X] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING: Donald H Rubin MD

TITLE IN ORGANIZATION: President

ADDRESS OF PERSON SIGNING: Avatar Biosci, Inc.
1937 Edenbridge Way
Nashville, TN 37215

SIGNATURE [signature] DATE 3.28.00

W053858.WPD

ATTORNEY DOCKET NO. 01123.0004

APPLICANT OR PATENTEE: Donald H. Rubin, Edward L. Organ and Raymond N. Dubois
FOR: **"MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION"**

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) and 1.27(d)) - NONPROFIT ORGANIZATION

I hereby declare that I am an official empowered to act on behalf of the nonprofit organization identified below:

NAME OF ORGANIZATION: VANDERBILT UNIVERSITY
ADDRESS OF ORGANIZATION: Office of Technology Transfer
1207 17^{th} Ave. S., Suite 210
Nashville, TN 37212

TYPE OF ORGANIZATION:

[X] University or other institution of higher education
(Name of state: Tennessee
(Citation of statute: ______________________________)
[ ] Tax exempt under Internal Revenue Service Code (26 USC 501(a) and 501(c)(3))
[ ] Non-profit scientific or educational under statute of state of the United States of America
(Name of state)
(Citation of statute)
[ ] Would qualify as tax exempt under Internal Revenue Service Code (26 USC 501(a) and 501(c) (3)) if it were located in The United States of America
[ ] Would qualify as nonprofit scientific or educational under statute of state of The United States of America if it were located in The United States of America
(Name of state)
(Citation of statute)

I hereby declare that the nonprofit organization identified above qualifies as a nonprofit organization as defined in 37 CFR 1.9 (e) for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code with regard to the invention entitled **"MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION"** by inventor(s) Donald H. Rubin, Edward L. Organ and Raymond N. Dubois filed concurrently herewith.

I hereby declare that rights under contract or law have been conveyed to and remain with the nonprofit organization with regard to the above identified invention.

If the rights held by the nonprofit organization are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR

1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

*NOTE: Separate verified statements are required for each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

NAME Avatar Biosci, Inc.

ADDRESS 1937 Edenbridge Way
Nashville, TN 37215

[ ]INDIVIDUAL [X] SMALL BUSINESS CONCERN [ ]NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING: JANIS ELSNER

TITLE IN ORGANIZATION: ASSOC. DIRECTOR

ADDRESS OF PERSON SIGNING: Vanderbilt University
Office of Technology Transfer
1207 17th Ave. S., Suite 210
Nashville, TN 37212

SIGNATURE: Janis Elsner DATE: Mar 29, 2000

ATTORNEY DOCKET NO. 01123.0004
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	
Rubin, Donald H. et al.	
Serial No.: Unassigned	Group Art Unit: Unassigned
Filed: Concurrently herewith	Examiner: Unassigned
For: **"MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION"**	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

NEEDLE & ROSENBERG, P.C.
Suite 1200, The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811

March 30, 2000

Sir:

Concurrently with the filing of this application, Applicants respectfully request entry of the following amendment:

IN THE SPECIFICATION:

On Page 1, at line 3 immediately after the title "Mammalian Genes Involved in Viral Infection and Tumor Suppression", please insert the following:

"This invention was made with partial government support under National Institutes of Health Grant No. CA68283 and a grant from the Department of Veterans Affairs. The United States Government has certain rights in the invention."

No fee is believed due; however, the Commissioner is hereby authorized to charge any deficiency to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

Janice A. Kimpel

Janice A. Kimpel
Registration No. 42,734

NEEDLE & ROSENBERG, P.C.
Suite 1200, The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811
404/688-0770

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mailing No. EL348124625US in an envelope addressed to: Assistant Commissioner for Patents, Box PCT, Washington, D.C. 20231, on this 30th day of March, 2000.

Janice A. Kimpel — March 30, 2000

Janice A. Kimpel — Date

MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION

BACKGROUND

Field of the Invention

The present invention provides methods of identifying cellular genes used for viral growth or for tumor progression. Thus, the present invention relates to nucleic acids related to and methods of reducing or preventing viral infection and for suppressing tumor progression. The invention also relates to methods for screening for additional such genes.

Background art

Various projects have been directed toward isolating and sequencing the genome of various animals, notably the human. However, most methodologies provide nucleotide sequences for which no function is linked or even suggested, thus limiting the immediate usefulness of such data.

The present invention, in contrast, provides methods of screening only for nucleic acids that are involved in a specific process, *i.e.*, viral infection or tumor progression. For viral infection, the nucleic acids isolated are useful in treatments for these processes because by this method only nucleic acids which are also nonessential to the cell are isolated. Such methods are highly useful, since they ascribe a function to each isolated gene, and thus the isolated nucleic acids can immediately be utilized in various specific methods and procedures.

For, example, the present invention provides methods of isolating nucleic acids encoding gene products used for viral infection, but nonessential to the cell. Viral infections are significant causes of human morbidity and mortality. Understanding the molecular mechanisms of such infections will lead to new approaches in their treatment and control.

Viruses can establish a variety of types of infection. These infections can be generally classified as lytic or persistent, though some lytic infections are considered persistent. Generally, persistent infections fall into two categories: (1) chronic (productive) infection, *i.e.*, infection wherein infectious virus is present and can be recovered by traditional biological methods and (2) latent infection, *i.e.*, infection

wherein viral genome is present in the cell but infectious virus is generally not produced except during intermittent episodes of reactivation. Persistence generally involves stages of both productive and latent infection.

Lytic infections can also persist under conditions where only a small fraction of the total cells are infected (smoldering (cycling) infection). The few infected cells release virus and are killed, but the progeny virus again only infect a small number of the total cells. Examples of such smoldering infections include the persistence of lactic dehydrogenase virus in mice (Mahy, B.W.J., *Br. Med. Bull.* 41: 50-55 (1985)) and adenovirus infection in humans (Porter, D.D. pp. 784-790 in Baron, S., ed. *Medical Microbiology* 2d ed. (Addison-Wesley, Menlo Park, CA 1985)).

Furthermore, a virus may be lytic for some cell types but not for others. For example, evidence suggests that human immunodeficiency virus (HIV) is more lytic for T cells than for monocytes/macrophages, and therefore can result in a productive infection of T cells that can result in cell death, whereas HIV-infected mononuclear phagocytes may produce virus for considerable periods of time without cell lysis. (Klatzmann, et al. *Science* 225:59-62 (1984); Koyanagi, et al. *Science* 241:1673-1675 (1988); Sattentau, et al. *Cell* 52:631-633 (1988)).

Traditional treatments for viral infection include pharmaceuticals aimed at specific virus derived proteins, such as HIV protease or reverse transcriptase, or recombinant (cloned) immune modulators (host derived), such as the interferons. However, the current methods have several limitations and drawbacks which include high rates of viral mutations which render anti-viral pharmaceuticals ineffective. For immune modulators, limited effectiveness, limiting side effects, a lack of specificity all limit the general applicability of these agents. Also the rate of success with current antivirals and immune-modulators has been disappointing.

One aspect of the current invention focuses on isolating genes that are not essential for cellular survival when disrupted in one or both alleles, but which are required for virus replication. This may occur with a dose effect, in which one allele knock-out may confer the phenotype of virus resistance for the cell. As targets for therapeutic intervention, inhibition of these cellular gene products, including: proteins, parts of proteins (modification enzymes that include, but are not restricted to glycosylation, lipid modifiers [myriolate, etc.]), lipids, transcription elements and RNA

regulatory molecules, may be less likely to have profound toxic side effects and virus mutation is less likely to overcome the 'block' to replicate successfully.

The present invention provides a significant improvement over previous methods of attempted therapeutic intervention against viral infection by addressing the cellular genes required by the virus for growth. Therefore, the present invention also provides an innovative therapeutic approach to intervention in viral infection by providing methods to treat viruses by inhibiting the cellular genes necessary for viral infection. Because these genes, by virtue of the means by which they are originally detected, are nonessential to the cell's survival at a level of expression necessary to inhibit virus replication, these treatment methods can be used in a subject without serious detrimental effects to the subject, as has been found with previous methods. The present invention also provides the surprising discovery that virally infected cells are dependent upon a factor in serum to survive. Therefore, the present invention also provides a method for treating viral infection by inhibiting this serum survival factor. Finally, these discoveries also provide a novel method for removing virally infected cells from a cell culture by removing, inhibiting or disrupting this serum survival factor in the culture so that non-infected cells selectively survive.

The selection of tumor suppressor gene(s) has become an important area in the discovery of new target for therapeutic intervention of cancer. Since the discovery that cells are restricted from promiscuous entry into the cell cycle by specific genes that are capable of suppressing a 'transformed' phenotype, considerable time has been invested in the discovery of such genes. Some of these genes include the gene associated by rhabdomyosarcoma (Rb) and the p53 (apoptosis related) encoding gene. The present invention provides a method, using gene-trapping, to select cell lines that have a transformed phenotype from cells that are not transformed and to isolate from these cells a gene that can suppress a malignant, or transformed, phenotype. Thus, by the nature of the isolation process, a function is associated with the isolated genes. The capacity to select quickly tumor suppressor genes can provide unique targets in the process of treating or preventing, and even for diagnostic testing of, cancer.

DETAILED DESCRIPTION OF THE INVENTION

The present invention utilizes a "gene trap" method along with a selection process to identify and isolate nucleic acids from genes associated with a particular function. Specifically, it provides a means of isolating cellular genes necessary for viral infection but not essential for the cell's survival, and it provides a means of isolating cellular genes that suppress tumor progression.

The present invention also provides a core discovery that virally infected cells become dependent upon at least one factor present in serum for survival, whereas non-infected cells do not exhibit this dependence. This core discovery has been utilized in the present invention in several ways. First, inhibition of the "serum survival factor" can be utilized to eradicate persistently virally infected cells from populations of non-infected cells. Inhibition of this factor can also be used to treat virus infection in a subject, as further described herein. Additionally, inhibition of or withdrawal of the serum survival factor in tissue culture allows for the detection of cellular genes required for viral replication yet nonessential for an uninfected cell to survive. The present invention further provides several such cellular genes, as well as methods of treating viral infections by inhibiting the functioning of such genes.

The invention also provides cellular genes whose overexpression is associated with inhibition of viral growth and/or reproduction.

The present method provides several cellular genes that are necessary for viral growth in the cell but are not essential for the cell to survive. These genes are important for lytic and persistent infection by viruses. These genes were isolated by generating gene trap libraries by infecting cells with a retrovirus gene trap vector, selecting for cells in which a gene trap event occurred (*i.e.*, in which the vector had inserted such that the promoterless marker gene was inserted such that a cellular promoter promotes transcription of the marker gene, *i.e.*, inserted into a functioning gene), starving the cells of serum, infecting the selected cells with the virus of choice while continuing serum starvation, and adding back serum to allow visible colonies to develop, which colonies were cloned by limiting dilution. Genes into which the retrovirus gene trap vector inserted were then isolated from the colonies using probes specific for the retrovirus gene trap vector. Thus nucleic acids isolated by this method are isolated portions of genes. Additionally, utilizing this method, several cellular genes were isolated whose

overexpression prevents viral infection or tumor growth, and they provide methods of treating viral infection or tumor growth/suppression by overexpression of these genes.

Thus the present invention provides a method of identifying a cellular gene necessary for viral growth in a cell and nonessential for cellular survival, comprising (a) transferring into a cell culture, *e.g.* growing in serum-containing medium, a vector encoding a selective marker gene lacking a functional promoter, (b) selecting cells expressing the marker gene, (c) removing serum from the culture medium, (d) infecting the cell culture with the virus, and (e) isolating from the surviving cells a cellular gene within which the marker gene is inserted, thereby identifying a gene necessary for viral growth in a cell and nonessential for cellular survival. The present invention also provides a method of identifying a cellular gene used for viral growth in a cell and nonessential for cellular survival, comprising (a) transferring into a cell culture growing in serum-containing medium a vector encoding a selective marker gene lacking a functional promoter, (b) selecting cells expressing the marker gene, (c) removing serum from the culture medium, (d) infecting the cell culture with the virus, and (e) isolating from the surviving cells a cellular gene within which the marker gene is inserted, thereby identifying a gene necessary for viral growth in a cell and nonessential for cellular survival or a gene whose overexpression prevents viral reproduction but is not fatal to the survival to the cell. In any selected cell type, such as Chinese hamster ovary cells, one can readily determine if serum starvation is required for selection. If it is not, serum starvation may be eliminated from the steps.

Alternatively, instead of removing serum from the culture medium, a serum factor required by the virus for growth can be inhibited, such as by the administration of an antibody that specifically binds that factor. Furthermore, if it is believed that there are no persistently infected cells in the culture, the serum starvation step can be eliminated and the cells grown in usual medium for the cell type. If serum starvation is used, it can be continued for a time after the culture is infected with the virus. Serum can then be added back to the culture. If some other method is used to inactivate the factor, it can be discontinued, inactivated or removed (such as removing the anti-factor antibody, *e.g.*, with a bound antibody directed against that antibody) prior to adding fresh serum back to the culture. Cells that survive are mutants having an inactivating insertion in a gene necessary for growth of the virus. The genes having the insertions can then be isolated by isolating sequences having the marker gene sequences. This mutational process

disturbs a wild type function. A mutant gene may produce at a lower level a normal product, it may produce a normal product not normally found in these cells, it may cause the overproduction of a normal product, it may produce an altered product that has some functions but not others, or it may completely disrupt a gene function. Additionally, the mutation may disrupt an RNA that has a function but is never translated into a protein. For example, the alpha-tropomyosin gene has a 3' RNA that is very important in cell regulation but never is translated into protein. (*Cell* 75 pg 1107-1117 , 12/17/93).

As used herein, a cellular gene "nonessential for cellular survival" means a gene for which disruption of one or both alleles results in a cell viable for at least a period of time which allows viral replication to be inhibited for preventative or therapeutic uses or use in research. A gene "necessary for viral growth" means the gene product, either protein or RNA, secreted or not, is necessary or beneficial, either directly or indirectly in some way for the virus to grow, and therefore, in the absence of that gene product (*i.e.*, a functionally available gene product), the virus does not spread. For example, such genes can encode cell cycle regulatory proteins, proteins affecting the vacuolar hydrogen pump, or proteins involved in protein folding and protein modification, including but not limited to: phosphorylation, methylation, glycosylation, myristylation or other lipid moiety, or protein processing via enzymatic processing. Some examples of such genes include vacuolar H+ATPase, alpha tropomyosin, gas5 gene, ras complex, N-acetyl-glucosaminy-l-transferase I mRNA, annexin II, c-golgi CM130 and calcyclin.

Any virus capable of infecting the cell can be used for this method. Virus can be selected based upon the particular infection desired to study. However, it is contemplated by the present invention that many viruses will be dependent upon the same cellular genes for survival; thus a cellular gene isolated using one virus can be used as a target for therapy for other viruses as well. Any cellular gene can be tested for relevancy to any desired virus using the methods set forth herein, *i.e.*, in general, by inhibiting the gene or its gene product in a cell and determining if the desired virus can grow in that cell. Some examples of viruses include HIV (including HIV-1 and HIV-2); parvovirus; papillomaviruses; hantaviruses; influenza viruses (*e.g.*, influenza A, B and C viruses); hepatitis viruses A to G; caliciviruses; astroviruses; rotaviruses; coronaviruses, such as human respiratory coronavirus; picornaviruses, such as human rhinovirus and enterovirus; ebola virus; human herpesvirus (*e.g.*, HSV-1-9); human adenovirus; for animal, the animal counterpart to any above listed human virus, animal retroviruses, such

as simian immunodeficiency virus, avian immunodeficiency virus, bovine immunodeficiency virus, feline immunodeficiency virus, equine infectious anemia virus, caprine arthritis encephalitis virus, arenaviruses, arvoviruses, tickborne viruses or visna virus.

The nucleic acids comprising cellular genes of this invention were isolated by the above method and as set forth in the examples. The invention includes a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127 (this list is sometimes referred to herein as "SEQ LIST 1" for brevity). Thus these nucleic acids can contain, in addition to the nucleotides set forth in each SEQ ID NO in the sequence listing, additional nucleotides at either end of the molecule. Such additional nucleotides can be added by any standard method, as known in the art, such as recombinant methods and synthesis methods. Examples of such nucleic acids comprising the nucleotide sequence set forth in any entry of the sequence listing contemplated by this invention include, but are not limited to, for example, the nucleic acid placed into a vector; a nucleic acid having one or

more regulatory region (*e.g.*, promoter, enhancer, polyadenylation site) linked to it, particularly in functional manner, *i.e.* such that an mRNA or a protein can be produced; a nucleic acid including additional nucleic acids of the gene, such as a larger or even full length genomic fragment of the gene, a partial or full length cDNA, a partial or full length RNA. Making and/or isolating such larger nucleic acids is further described below and is well known and standard in the art.

Also provided in this invention are the double-stranded nucleic acids corresponding to the nucleic acid sequences set forth in SEQ ID 1 through SEQ ID 136, inclusive. It is recognized that "nucleic acid" as used herein, can refer to either or both strands of such double-stranded nucleic acids, such strands often referred to as the "positive" and "negative" strands. Either strand of such double-stranded nucleic acids may encode the polypeptides of this invention, and the coding sequences for such polypeptides may be translated in either direction along the strand. Examples of polypeptides encoded by either strand are disclosed herein.

The invention also provides a nucleic acid encoding the protein encoded by the gene comprising the nucleotide sequence set forth in any of the sequences listed in SEQ LIST 1, as well as allelic variants and homologs of each such gene. The gene is readily obtained using standard methods, as described below and as is known and standard in the art. The present invention also contemplates any unique fragment of these genes or of the nucleic acids set forth in any of the sequences listed in SEQ LIST 1. Examples of inventive fragments of the inventive genes can include the nucleic acids whose sequence is set forth in any of the sequences listed in SEQ LIST 1. To be unique, the fragment must be of sufficient size to distinguish it from other known sequences, most readily determined by comparing any nucleic acid fragment to the nucleotide sequences of nucleic acids in computer databases, such as GenBank. Such comparative searches are standard in the art. Typically, a unique fragment useful as a primer or probe will be at least about 20 to about 25 nucleotides in length, depending upon the specific nucleotide content of the sequence. Additionally, fragments can be, for example, at least about 30, 40, 50, 75, 100, 200 or 500 nucleotides in length. The nucleic acids can be single or double stranded, depending upon the purpose for which it is intended.

The present invention further provides a nucleic acid comprising the regulatory region of a gene comprising any one of the nucleotide sequences set forth in SEQ LIST 1, as well as homologs of each such gene. Additionally provided is a construct

comprising such a regulatory region functionally linked to a reporter gene. Such reporter gene constructs can be used to screen for compounds and compositions that affect expression of the gene comprising the nucleic acids whose sequence is set forth in SEQ LIST 1, or any homologs thereof.

The nucleic acids set forth in the sequence listing are gene fragments; the entire coding sequence and the entire gene that comprises each fragment are both contemplated herein and are readily obtained by standard methods, given the nucleotide sequences presented in the sequence listing (*see. e.g.,* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989; *DNA cloning: A Practical Approach*, Volumes I and II, Glover, D.M. ed., IRL Press Limited, Oxford, 1985). To obtain the entire genomic gene, briefly, a nucleic acid whose sequence is set forth in any of SEQ ID NO:1 through SEQ ID NO:127, or preferably in any of the sequences listed in SEQ LIST 1, or a smaller fragment thereof, is utilized as a probe to screen a genomic library under high stringency conditions, and isolated clones are sequenced. Once the sequence of the new clone is determined, a probe can be devised from a portion of the new clone not present in the previous fragment and hybridized to the library to isolate more clones containing fragments of the gene. In this manner, by repeating this process in organized fashion, one can "walk" along the chromosome and eventually obtain nucleotide sequence for the entire gene. Similarly, one can use portions of the present fragments, or additional fragments obtained from the genomic library, that contain open reading frames to screen a cDNA library to obtain a cDNA having the entire coding sequence of the gene. Repeated screens can be utilized as described above to obtain the complete sequence from several clones if necessary. The isolates can then be sequenced to determine the nucleotide sequence by standard means such as dideoxynucleotide sequencing methods (*see, e.g.*, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989).

The present genes were isolated from rat; however, homologs in any desired species, preferably mammalian, such as human, can readily be obtained by screening a human library, genomic or cDNA, with a probe comprising sequences of the nucleic acids set forth in the sequence listing herein, or fragments thereof, and isolating genes specifically hybridizing with the probe under preferably relatively high stringency hybridization conditions. For example, high salt conditions (*e.g.,* in 6X SSC or 6X

SSPE) and/or high temperatures of hybridization can be used. For example, the stringency of hybridization is typically about 5°C to 20°C below the T_m (the melting temperature at which half of the molecules dissociate from its partner) for the given chain length. As is known in the art, the nucleotide composition of the hybridizing region factors in determining the melting temperature of the hybrid. For 20mer probes, for example, the recommended hybridization temperature is typically about 55-58°C. Additionally, the rat sequence can be utilized to devise a probe for a homolog in any specific animal by determining the amino acid sequence for a portion of the rat protein, and selecting a probe with optimized codon usage to encode the amino acid sequence of the homolog in that particular animal. Any isolated gene can be confirmed as the targeted gene by sequencing the gene to determine it contains the nucleotide sequence listed herein as comprising the gene. Any homolog can be confirmed as a homolog by its functionality.

Additionally contemplated by the present invention are nucleic acids, from any desired species, preferably mammalian and more preferably human, having 98%, 95%, 90%, 85%, 80%, 70%, 60%, or 50% homology, or greater, in the region of homology, to a region in an exon of a nucleic acid encoding the protein encoded by the gene comprising the nucleotide sequence set forth in any of the sequences listed in SEQ LIST 1 or to homologs thereof. Also contemplated by the present invention are nucleic acids, from any desired species, preferably mammalian and more preferably human, having 98%, 95%, 90%, 85%, 80%, 70%, 60%, or 50% homology, or greater, in the region of homology, to a region in an exon of a nucleic acid comprising the nucleotide sequence set forth in any of the sequences listed in SEQ LIST 1 or to homologs thereof. These genes can be synthesized or obtained by the same methods used to isolate homologs, with stringency of hybridization and washing, if desired, reduced accordingly as homology desired is decreased, and further, depending upon the G-C or A-T richness of any area wherein variability is searched for. Allelic variants of any of the present genes or of their homologs can readily be isolated and sequenced by screening additional libraries following the protocol above. Methods of making synthetic genes are described in U.S. Patent No. 5,503,995 and the references cited therein.

The nucleic acid encoding any selected protein of the present invention can be any nucleic acid that functionally encodes that protein. For example, to functionally encode, *i.e.*, allow the nucleic acid to be expressed, the nucleic acid can include, for

example, exogenous or endogenous expression control sequences, such as an origin of replication, a promoter, an enhancer, and necessary information processing sites, such as ribosome binding sites, RNA splice sites, polyadenylation sites, and transcriptional terminator sequences. Preferred expression control sequences can be promoters derived from metallothionine genes, actin genes, immunoglobulin genes, CMV, SV40, adenovirus, bovine papilloma virus, etc. Expression control sequences can be selected for functionality in the cells in which the nucleic acid will be placed. A nucleic acid encoding a selected protein can readily be determined based upon the amino acid sequence of the selected protein, and, clearly, many nucleic acids will encode any selected protein.

The present invention additionally provides a nucleic acid that selectively hybridizes under stringent conditions with a nucleic acid set forth in SEQ LIST 1 or with a nucleic acid encoding the protein encoded by the gene comprising the nucleotide sequence set forth in any sequence listed in SEQ LIST 1. This hybridization can be specific. The degree of complementarity between the hybridizing nucleic acid and the sequence to which it hybridizes should be at least enough to exclude hybridization with a nucleic acid encoding an unrelated protein. Thus, a nucleic acid that selectively hybridizes with a nucleic acid of the present protein coding sequence will not selectively hybridize under stringent conditions with a nucleic acid for a different, unrelated protein, and vice versa. Typically, the stringency of hybridization to achieve selective hybridization involves hybridization in high ionic strength solution (6X SSC or 6X SSPE) at a temperature that is about 12-25°C below the T_m (the melting temperature at which half of the molecules dissociate from its partner) followed by washing at a combination of temperature and salt concentration chosen so that the washing temperature is about 5°C to 20°C below the T_m of the hybrid molecule. The temperature and salt conditions are readily determined empirically in preliminary experiments in which samples of reference DNA immobilized on filters are hybridized to a labeled nucleic acid of interest and then washed under conditions of different stringencies. Hybridization temperatures are typically higher for DNA-RNA and RNA-RNA hybridizations. The washing temperatures can be used as described above to achieve selective stringency, as is known in the art. (Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989; Kunkel et al. *Methods Enzymol.* 1987:154:367, 1987). Nucleic acid fragments that selectively hybridize to any

given nucleic acid can be used, *e.g.*, as primers and or probes for further hybridization or for amplification methods (*e.g.*, polymerase chain reaction (PCR), ligase chain reaction (LCR)) . A preferable stringent hybridization condition for a DNA:DNA hybridization can be at about 68°C (in aqueous solution) in 6X SSC or 6X SSPE followed by washing at 68°C.

The present invention additionally provides a polypeptide comprising the amino acid sequence encoded by the gene comprising the nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127 (*i.e.*, SEQ LIST 1). Additionally, polypeptides comprising the amino acid sequence encoded by a nucleic acid that selectively hybridizes under stringent conditions with a nucleic acid in SEQ LIST 1 are provided. Further, polypeptides comprising the amino acid sequence encoded by a nucleic acid having a region within an exon wherein the region has at least 50, 60, 70, 80, 90, or 95% homology with a nucleic acid in SEQ LIST 1. These polypeptides can be readily obtained by any of several means. For example, the nucleotide sequence of coding regions of the gene can be translated and then the

corresponding polypeptide can be synthesized mechanically by standard methods. Additionally, the coding regions of the genes can be expressed or synthesized, an antibody specific for the resulting polypeptide can be raised by standard methods (see, *e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1988), and the protein can be isolated from other cellular proteins by selective hybridization with the antibody. This protein can be purified to the extent desired by standard methods of protein purification (see, *e.g.*, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989). The amino acid sequence of any protein, polypeptide or peptide of this invention can be deduced from the nucleic acid sequence, or it can be determined by sequencing an isolated or recombinantly produced protein.

The terms "peptide," "polypeptide"and "protein" can be used interchangeably herein and refer to a polymer of amino acids and includes full-length proteins and fragments thereof. As used in the specification and in the claims, "a" can mean one or more, depending upon the context in which it is used. An amino acid residue is an amino acid formed upon chemical digestion (hydrolysis) of a polypeptide at its peptide linkages. The amino acid residues described herein are preferably in the L isomeric form. However, residues in the D isomeric form can be substituted for any L-amino acid residue, as long as the desired functional property is retained by the polypeptide. Standard polypeptide nomenclature (described in *J. Biol. Chem.*, 243:3552-59 (1969) and adopted at 37 CFR § 1.822(b)) is used herein.

As will be appreciated by those skilled in the art, the invention also includes those polypeptides having slight variations in amino acid sequences or other properties. Amino acid substitutions can be selected by known parameters to be neutral (*see, e.g.,* Robinson WE Jr, and Mitchell WM., AIDS 4:S151-S162(1990)). Such variations may arise naturally as allelic variations (*e.g.,* due to genetic polymorphism) or may be produced by human intervention (*e.g.,* by mutagenesis of cloned DNA sequences), such as induced point, deletion, insertion and substitution mutants. Minor changes in amino acid sequence are generally preferred, such as conservative amino acid replacements, small internal deletions or insertions, and additions or deletions at the ends of the molecules. Substitutions may be designed based on, for example, the model of Dayhoff, *et al.* (in *Atlas of Protein Sequence and Structure 1978,* Nat'l Biomed. Res. Found., Washington,

D.C.). These modifications can result in changes in the amino acid sequence, provide silent mutations, modify a restriction site, or provide other specific mutations. Likewise, such amino acid changes result in a different nucleic acid encoding the polypeptides and proteins. Thus, alternative nucleic acids are also contemplated by such modifications.

The present invention also provides cells containing a nucleic acid of the invention. A cell containing a nucleic acid encoding a protein typically can replicate the DNA and, further, typically can express the encoded protein. The cell can be a prokaryotic cell, particularly for the purpose of producing quantities of the nucleic acid, or a eukaryotic cell, particularly a mammalian cell. The cell is preferably a mammalian cell for the purpose of expressing the encoded protein so that the resultant produced protein has mammalian protein processing modifications.

Nucleic acids of the present invention can be delivered into cells by any selected means, in particular depending upon the purpose of the delivery of the compound and the target cells. Many delivery means are well-known in the art. For example, electroporation, calcium phosphate precipitation, microinjection, cationic or anionic liposomes, and liposomes in combination with a nuclear localization signal peptide for delivery to the nucleus can be utilized, as is known in the art.

The present invention also contemplates that the mutated cellular genes necessary for viral growth, produced by the present method, as well as cells containing these mutants can also be useful. These mutated genes and cells containing them can be isolated and/or produced according to the methods herein described and using standard methods.

It should be recognized that the sequences set forth herein may contain minor sequencing errors. Such errors can be corrected, for example, by using the hybridization procedure described above with various probes derived from the described sequences such that the coding sequence can be reisolated and resequenced.

As described in the examples, the present invention provides the discovery of a "serum survival factor" present in serum that is necessary for the survival of persistently virally infected cells. Isolation and characterization of this factor have shown it to be a protein, to have a molecular weight of between about 50 kD and 100 kD, to resist inactivation in low pH (*e.g.*, pH2) and chloroform extraction, to be inactivated by boiling for about 5 minutes and in low ionic strength solution (*e.g.*, about 10 mM to about 50 mM). The present invention thus provides a purified mammalian serum protein having a

molecular weight of between about 50 kD and 100 kD which resists inactivation in low pH and resists inactivation by chloroform extraction, which inactivates when boiled and inactivates in low ionic strength solution, and which when removed from a cell culture comprising cells persistently infected with reovirus selectively substantially prevents survival of cells persistently infected with reovirus. The factor, fitting the physical characteristics described above, can readily be verified by adding it to non-serum-containing medium (which previously could not support survival of persistently virally infected cells) and determining whether this medium with the added putative factor can now support persistently virally infected cells, particularly cells persistently infected with reovirus. As used herein, a "purified" protein means the protein is at least of sufficient purity such that an approximate molecular weight can be determined.

The amino acid sequence of the protein can be elucidated by standard methods. For example, an antibody to the protein can be raised and used to screen an expression library to obtain nucleic acid sequence coding the protein. This nucleic acid sequence is then simply translated into the corresponding amino acid sequence. Alternatively, a portion of the protein can be directly sequenced by standard amino acid sequencing methods (amino-terminus sequencing). This amino acid sequence can then be used to generate an array of nucleic acid probes that encompasses all possible coding sequences for a portion of the amino acid sequence. The array of probes is used to screen a cDNA library to obtain the remainder of the coding sequence and thus ultimately the corresponding amino acid sequence.

The present invention also provides methods of detecting and isolating additional serum survival factors. For example, to determine if any known serum components are necessary for viral growth, the known components can be inhibited in, or eliminated from, the culture medium, and it can be observed whether viral growth is inhibited by determining if persistently infected cells do not survive. One can add the factor back (or remove the inhibition) and determine whether the factor allows for viral growth.

Additionally, other, unknown serum components can also be found to be essential for growth. Serum can be fractionated by various standard means, and fractions added to serum free medium to determine if a factor is present in a reaction that allows growth previously inhibited by the lack of serum. Fractions having this activity can then be further fractionated until the factor is relatively free of other components. The factor can then be characterized by standard methods, such as size fractionation, denaturation and/or

inactivation by various means, etc. Preferably, once the factor has been purified to a desired level of purity, it is added to cells in serum free medium to confirm that it bestows the function of allowing virus to grow when serum-free medium alone did not. This method can be repeated to confirm the requirement for the specific factor for any desired virus, since each serum factor found to be required by any one virus can also be required by many other viruses. In general, the closer the viruses are related and the more similar the infection modes of the viruses, the more likely that a factor required by one virus will be required by the other.

The present invention also provides methods of treating virus infections utilizing applicants' discoveries. The subject of any of the herein described methods can be any animal, preferably a mammal, such as a human, a veterinary animal, such as a cat, dog, horse, pig, goat, sheep, or cow, or a laboratory animal, such as a mouse, rat, rabbit, or guinea pig, depending upon the virus.

The present invention provides a method of reducing or inhibiting, and thereby treating, a viral infection in a subject, comprising administering to the subject an inhibiting amount of a composition that inhibits functioning of the serum protein described herein, *i.e.* the serum protein having a molecular weight of between about 50 kD and 100 kD which resists inactivation in low pH and resists inactivation by chloroform extraction, which inactivates when boiled and inactivates in low ionic strength solution, and which when removed from a cell culture comprising cells persistently infected with the virus prevents survival of at least some cells persistently infected with the virus, thereby treating the viral infection. The composition can comprise, for example, an antibody that specifically binds the serum protein, or an antisense RNA that binds an RNA encoded by a gene functionally encoding the serum protein.

Any virus capable of infecting the selected subject to be treated can be treated by the present methods. As described above, any serum protein or survival factor found by the present methods to be necessary for growth of cells infected with any one virus can be found to be necessary for growth of the cells infected with many other viruses. For any given cell-virus combination, the serum protein or factor can be confirmed to be required for growth by the methods described herein. The cellular genes identified by the examples using reovirus, a mammalian pathogen, and a rat cell system have general applicability to other virus infections that include all of the known as well as yet to be discovered human pathogens, including, but not limited to: human immunodeficiency

viruses (*e.g.*, HIV-1, HIV-2); parvovirus; papillomaviruses; hantaviruses; influenza viruses (*e.g.,* influenza A, B and C viruses); hepatitis viruses A to G; caliciviruses; astroviruses; rotaviruses; coronaviruses, such as human respiratory coronavirus; picornaviruses, such as human rhinovirus and enterovirus; ebola virus; human herpesvirus (*e.g.*, HSV-1-9); human adenovirus; hantaviruses; for animal, the animal counterpart to any above listed human virus, animal retroviruses, such as simian immunodeficiency virus, avian immunodeficiency virus, bovine immunodeficiency virus, feline immunodeficiency virus, equine infectious anemia virus, caprine arthritis encephalitis virus, arenaviruses, arvoviruses, tickborne virus or visna virus.

A protein inhibiting amount of the composition can be readily determined, such as by administering varying amounts to cells or to a subject and then adjusting the effective amount for inhibiting the protein according to the volume of blood or weight of the subject. Compositions that bind to the protein can be readily determined by running the putatively bound protein on a protein gel and observing an alteration in the protein's migration through the gel. Inhibition of the protein can be determined by any desired means such as adding the inhibitor to complete media used to maintain persistently infected cells and observing the cells' viability. The composition can comprise, for example, an antibody that specifically binds the serum protein. Specific binding by an antibody means that the antibody can be used to selectively remove the factor from serum or inhibit the factor's biological activity and can readily be determined by radio immune assay (RIA), bioassay, or enzyme-linked immunosorbant (ELISA) technology. The composition can comprise, for example, an antisense RNA that specifically binds an RNA encoded by the gene encoding the serum protein. Antisense RNAs can be synthesized and used by standard methods (*e.g., Antisense RNA and DNA*, D. A. Melton, Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1988)).

The present methods provide a method of screening a compound for effectiveness in treating or preventing a viral infection, comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product necessary for reproduction of the virus in the cell but not necessary for survival of the cell and detecting the level and/or activity (i.e. function) of the gene product produced, a decrease or elimination of the gene product and/or the gene product activity indicating a compound for treating or preventing the viral infection. The cellular gene can be, for example, a nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ

ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82; SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127 (herein sometimes referred to as SEQ LIST 2, for brevity), any homolog thereof, or any other gene obtained using the methods provided herein for obtaining such genes. It is understood that the cellular gene can be present naturally in the cell being screened, or it can be introduced into the cell in a suitable expression vector, as are well known in the art. The level of the gene product can be measured by any standard means, such as by detection with an antibody specific for the protein. The level of gene product can be compared to the level of the gene product in a control cell not contacted with the compound. The level of gene product can be compared to the level of the gene product in the same cell prior to addition of the compound. Activity, or function, can be measured by any standard means, such as by enzymatic assays that measure the conversion of a substrate to a product or binding

assays that measure the binding of a protein to a nucleic acid, for example. Examples of gene products disclosed herein whose activity/function can be measured include tristetraprolin (human ZFP-36), 6-pyruvoyl-tetrahydropterin synthase, a eukaryotic DnaJ-like protein, ID3 (inhibitor of DNA binding 3), N-acetylglucos-aminyltransferase I (mGAT-1), cleavage stimulation factor (CSTF2), TAK1 binding protein, human zinc transcription factor ZPF207, Dlx2, Smad7 (Mad-related protein), and P-glycoprotein (mdr1b). The activity can be compared to the activity in a control cell not contacted with the compound or in the same cell prior to addition of the compound. Relatedly, the regulatory region of the gene can be functionally linked to a reporter gene and compounds can be screened for inhibition of the reporter gene. Such reporter constructs are described herein.

The present invention also provides a method of screening a compound for effectiveness in treating or preventing a viral infection comprising contacting the compound with the gene product of a cellular gene comprising a nucleic acid of SEQ LIST 2, or any homolog thereof, and detecting the function of the gene product, a decrease or elimination of the function indicating a compound effective for treating or preventing viral infection. Examples of gene products disclosed herein that can be utilized in this method include tristetraprolin (human ZFP-36), 6-pyruvoyl-tetrahydropterin synthase, a eukaryotic DnaJ-like protein, ID3 (inhibitor of DNA binding 3), N-acetylglucos-aminyltransferase I (mGAT-1), cleavage stimulation factor (CSTF2), TAK1 binding protein, human zinc transcription factor ZPF207, Dlx2, Smad7 (Mad-related protein), and P-glycoprotein (mdr1b).

The present invention provides a method of selectively eliminating cells persistently infected with a virus from an animal cell culture capable of surviving for a first period of time in the absence of serum, comprising propagating the cell culture in the absence of serum for a second time period during which a persistently infected cell cannot survive without serum, thereby selectively eliminating from the cell culture cells persistently infected with the virus. The second time period should be shorter than the first time period. Thus one can simply eliminate serum from a standard culture medium composition for a period of time (*e.g.* by removing serum containing medium from the culture container, rinsing the cells, and adding serum-free medium back to the container), then, after a time of serum starvation, return serum to the culture medium. Alternatively, one can inhibit a serum survival factor from the culture in place of the step of serum starvation. Furthermore, one can instead interfere with the virus-factor interaction. Such a

viral elimination method can periodically be performed for cultured cells to ensure that they remain virus-free. The time period of serum removal can greatly vary, with a typical range being about 1 to about 30 days; a preferable period can be about 3 to about 10 days, and a more preferable period can be about 5 days to about 7 days. This time period can be selected based upon ability of a specific cell to survive without serum as well as the life cycle of the target virus, *e.g.*, for reovirus, which has a life cycle of about 24 hours, 3 days' starvation of cells provides dramatic results.

Furthermore, the time period can be shortened by also passaging the cells during the starvation; in general, increasing the number of passages can decrease the time of serum starvation (or serum factor inhibition) needed to get full clearance of the virus from the culture. While passaging, the cells typically are exposed briefly to serum (typically for about 3 to about 24 hours). This exposure both stops the action of the trypsin used to dislodge the cells and stimulates the cells into another cycle of growth, thus aiding in this selection process. Thus a starvation/serum cycle can be repeated to optimize the selective effect. Other standard culture parameters, such as confluency of the cultures, pH, temperature, etc. can be varied to alter the needed time period of serum starvation (or serum survival factor inhibition). This time period can readily be determined for any given viral infection by simply removing the serum for various periods of time, then testing the cultures for the presence of the infected cells (*e.g.*, by ability to survive in the absence of serum and confirmed by quantitating virus in cells by standard virus titration and immunohistochemical techniques) at each tested time period, and then detecting at which time periods of serum deprivation the virally infected cells were eliminated. It is preferable that shorter time periods of serum deprivation that still provide elimination of the persistently infected cells be used. Furthermore, the cycle of starvation, then adding back serum and determining amount of virus remaining in the culture can be repeated until no virtually infected cells remain in the culture.

Thus, the present method can further comprise passaging the cells, *i.e.*, transferring the cell culture from a first container to a second container. Such transfer can facilitate the selective lack of survival of virally infected cells. Transfer can be repeated several times. Transfer is achieved by standard methods of tissue culture (*see, e.g.*, Freshney, *Culture of Animal Cells, A Manual of Basic Technique*, 2nd Ed. Alan R. Liss, Inc., New York, 1987).

The present method further provides a method of selectively eliminating from a cell culture cells persistently infected with a virus, comprising propagating the cell culture

in the absence of a functional form of the serum protein having a molecular weight of between about 50 kD and 100 kD which resists inactivation in low pH and resists inactivation by chloroform extraction, which inactivates when boiled and inactivates in low ionic strength solution, and which when removed from a cell culture comprising cells persistently infected with reovirus substantially prevents survival of cells persistently infected with reovirus. The absence of the functional form can be achieved by any of several standard means, such as by binding the protein to an antibody selective for it (binding the antibody in serum either before or after the serum is added to the cells; if before, the serum protein can be removed from the serum by, *e.g.*, binding the antibody to a column and passing the serum over the column and then administering the survival protein-free serum to the cells), by administering a compound that inactivates the protein, or by administering a compound that interferes with the interaction between the virus and the protein.

Thus, the present invention provides a method of selectively eliminating from a cell culture propagated in serum-containing medium cells persistently infected with a virus, comprising inhibiting in the serum the protein having a molecular weight of between about 50 kD and 100 kD which resists inactivation in low pH and resists inactivation by chloroform extraction, which inactivates when boiled and inactivates in low ionic strength solution, and which when removed from a cell culture comprising cells persistently infected with reovirus substantially prevents survival of cells persistently infected with reovirus. Alternatively, the interaction between the virus and the serum protein can be disrupted to selectively eliminate cells persistently infected with the virus.

Any virus capable of some form of persistent infection may be eliminated from a cell culture utilizing the present elimination methods, including removing, inhibiting or otherwise interfering with a serum protein, such as the one exemplified herein, and also including removing, inhibiting or otherwise interfering with a gene product from any cellular gene found by the present method to be necessary for viral growth yet nonessential to the cell. For example, DNA viruses or RNA viruses can be targeted. One can readily determine whether cells infected with a selected virus can be selectively removed from a culture through removal of serum by starving cells permissive to the virus of serum (or inhibiting the serum survival factor), adding the selected virus to the cells, adding serum to the culture, and observing whether infected cells die (*i.e.*, by titering levels of virus in the surviving cells with an antibody specific for the virus).

A culture of any animal cell (*i.e.*, any cell that is typically grown and maintained in culture in serum) that can be maintained for a period of time in the absence of serum, can be purified from viral infection utilizing the present method. For example, primary cultures as well as established cultures and cell lines can be used. Furthermore, cultures of cells from any animal and any tissue or cell type within that animal that can be cultured and that can be maintained for a period of time in the absence of serum can be used. For example, cultures of cells from tissues typically infected, and particularly persistently infected, by an infectious virus could be used.

As used in the claims "in the absence of serum" means at a level at which persistently virally infected cells do not survive. Typically, the threshold level is about 1% serum in the media. Therefore, about 1% serum or less can be used, such as about 1%, 0.75%, 0.50%. 0.25% 0.1% or no serum can be used.

As used herein, "selectively eliminating" cells persistently infected with a virus means that substantially all of the cells persistently infected with the virus are killed such that the presence of virally infected cells cannot be detected in the culture immediately after the elimination procedure has been performed. Furthermore, "selectively eliminating" includes that cells not infected with the virus are generally not killed by the method. Some surviving cells may still produce virus but at a lower level, and some may be defective in pathways that lead to death by the virus. Typically, for cells persistently infected with virus to be substantially all killed, more than about 90% of the cells, and more preferably more than about 95%, 98%, 99%, or 99.99% of virus-containing cells in the culture are killed.

The present method also provides a nucleic acid comprising the regulatory region of any of the genes. Such regulatory regions can be isolated from the genomic sequences isolated and sequenced as described above and identified by any characteristics observed that are characteristic for regulatory regions of the species and by their relation to the start codon for the coding region of the gene. The present invention also provides a construct comprising the regulatory region functionally linked to a reporter gene. Such constructs are made by routine subcloning methods, and many vectors are available into which regulatory regions can be subcloned upstream of a marker gene. Marker genes can be chosen for ease of detection of marker gene product.

The present method therefore also provides a method of screening a compound for treating a viral infection, comprising administering the compound to a cell containing any

of the above-described constructs, comprising a regulatory region of one of the genes comprising any of the nucleotide sequences set forth in SEQ LIST 2, or any homologs thereof, whose inhibition or reduction in expression causes inhibition of viral replication wherein the region is functionally linked to a reporter gene, and detecting the level of the reporter gene product produced, a decrease or elimination of the reporter gene product indicating a compound for treating the viral infection. Compounds detected by this method would inhibit transcription of the gene from which the regulatory region was isolated, and thus, in treating a subject, would inhibit the production of the gene product produced by the gene, and thus treat the viral infection.

Some genes when disrupted by the present method of retrovirus insertion, resulted in over expression of the gene product, and this overexpression inhibited viral replication. Thus the present invention provides a method of screening a compound for effectiveness in treating a viral infection, comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product whose overexpression inhibits reproduction of the virus but does not prevent survival of the cell and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for treating the viral infection. Typically, an increase will be a 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 125%, 150%, 175%, 200%, 300%, 400%, 500% or higher increase over gene product produced when the compound is not present.

The present invention additionally provides a method of reducing or inhibiting a viral infection in a subject, comprising administering to the subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid set forth in any of SEQ LIST 2, or a homolog thereof, thereby treating the viral infection. Reducing or inhibiting viral infection naturally can include both the initial infection of the subject and the infection of uninfected cells within an already infected subject, e.g. inhibiting viral replication in cells of the subject. The composition can comprise, for example, an antibody that binds a protein encoded by the gene. The composition can also comprise an antibody that binds a receptor for a protein encoded by the gene. Such an antibody can be raised against the selected protein by standard methods as set forth above, and can be either polyclonal or monoclonal, though monoclonal is preferred. Alternatively, the composition can comprise an antisense RNA that binds an RNA encoded by the gene, as described above. Examples of antisense RNA useful therapeutically include the fragments of the nucleic acids described above.

Furthermore, the composition can comprise a nucleic acid functionally encoding an antisense RNA that binds an RNA encoded by the gene. Other useful compositions will be readily apparent to the skilled artisan.

The present invention also provides a method of treating a viral infection in a subject comprising administering to the subject a treatment effective amount of a composition that increases expression of a gene whose over expression reduces or inhibits viral replication. Typically, an increase will be a 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 125%, 150%, 175%, 200%, 300%, 400%, 500% or higher increase over gene product produced when the composition is not present.

The present invention further provides a method of reducing or inhibiting a viral infection in a subject comprising mutating *ex vivo* in a selected cell, for example from the subject or from an allogenic source, an endogenous gene comprising a nucleic acid set forth in SEQ LIST 2 whose inhibition or reduction in expression causes inhibition of viral replication, or a homolog thereof, to a gene form incapable of producing a functional gene product of the gene or a gene form producing a reduced amount of a functional gene product of the gene, and placing (or replacing, in the case of the subject's own cells) the cell in the subject, thereby reducing viral infection of cells in the subject. The cell can be selected according to the typical target cell of the specific virus whose infection is to be reduced, prevented or inhibited. A preferred cell for several viruses is a hematopoietic cell. When the selected cell is a hematopoietic cell, viruses which can be reduced or inhibited from infection can include, for example, HIV, including HIV-1 and HIV-2. However, many other virus-cell combinations will be apparent to the skilled artisan.

The invention also includes a method of reducing or inhibiting viral infection in a subject comprising mutating *ex vivo* in a selected cell, for example from a subject or an allogenic source, an endogenous gene comprising a nucleic acid set forth in SEQ LIST 2 whose overexpression causes inhibition of viral replication, or a homolog thereof, to a gene form that expresses the gene at a higher level than the endogenous gene, and placing or replacing the cell in the subject. Typically, a higher level can be 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 125%, 150%, 175%, 200%, 300%, 400%, 500% or higher than the non-mutated, endogenous gene. The cell can be selected according to the typical target cell of the specific virus whose infection is to be reduced, prevented or inhibited. A preferred cell for several viruses is a hematopoietic cell. When the selected cell is a hematopoietic cell, viruses which can be reduced or inhibited from infection can

include, for example, HIV, including HIV-1 and HIV-2. However, many other virus-cell combinations will be apparent to the skilled artisan.

The present invention additionally provides a method of increasing viral infection resistance in a subject comprising mutating *ex vivo* in a selected cell, for example from the subject or from an allogenic source, an endogenous gene comprising a nucleic acid set forth in SEQ LIST 2, whose inhibition or reduction in expression increases viral infection resistance, said endogenous gene being mutated to a mutated gene form incapable of producing a functional gene product of the gene or a gene form producing a reduced amount of a functional gene product of the gene, and placing the cell in the subject, thereby increasing viral infection resistance of cells in the subject. The virus can be HIV, particularly when the cell is a hematopoietic cell. However, many other virus-cell combinations will be apparent to the skilled artisan.

Furthermore, the present invention provides a method for isolation of cellular genes utilized in tumor progression. The present invention provides a method of identifying a cellular gene that can suppress a malignant phenotype in a cell, comprising (a) transferring into a cell culture incapable of growing well in soft agar or Matrigel a vector encoding a selective marker gene lacking a functional promoter, (b) selecting cells expressing the marker gene, and (c) isolating from selected cells which are capable of growing in soft agar or Matrigel a cellular gene within which the marker gene is inserted, thereby identifying a gene that can suppress a malignant phenotype in a cell. This method can be performed using any selected non-transformed cell line, of which many are known in the art.

The present invention additionally provides a method of identifying a cellular gene that can suppress a malignant phenotype in a cell, comprising (a) transferring into a cell culture of non-transformed cells a vector encoding a selective marker gene lacking a functional promoter, (b) selecting cells expressing the marker gene, and (c) isolating from selected and transformed cells a cellular gene within which the marker gene is inserted, thereby identifying a gene that can suppress a malignant phenotype in a cell. A non-transformed phenotype can be determined by any of several standard methods in the art, such as the exemplified inability to grow in soft agar, or inability to grow in Matrigel.

The present invention further provides a method of screening for a compound for suppressing a malignant phenotype in a cell comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product involved in

establishment of a malignant phenotype in the cell and detecting the level of the gene product produced, a decrease, inhibition or elimination of the gene product indicating a compound effective for suppressing the malignant phenotype. Detection of the level, or amount, of gene product produced can be measured, directly or indirectly, by any of several methods standard in the art (*e.g.*, protein gel, antibody-based assay, detecting labeled RNA) for assaying protein levels or amounts, and selected based upon the specific gene product.

The present invention also provides a method of screening for a compound for suppressing a malignant phenotype in a cell comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product whose overexpression is involved in suppressing a malignant phenotype in the cell and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for suppressing the malignant phenotype.

The present invention further provides a method of suppressing a malignant phenotype in a cell in a subject, comprising administering to the subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid set forth in SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:36 or SEQ ID NO:94, or a homolog thereof, or any gene whose overexpression is found by the present method to be involved in suppressing a malignant phenotype in the cell (e.g., any clone designated herein with an "x") thereby suppressing a malignant phenotype. The composition can, for example, comprise an antibody that binds a protein encoded by the gene. The composition can, as another example, comprise an antibody that binds a receptor for a protein encoded by the gene. The composition can comprise an antisense RNA that binds an RNA encoded by the gene. Further, the composition can comprise a nucleic acid functionally encoding an antisense RNA that binds an RNA encoded by the gene.

The present invention further provides a method of suppressing a malignant phenotype in a cell in a subject, comprising administering to the subject an amount of a composition that increases expression of a gene product whose overexpression is involved in suppressing a malignant phenotype in the cell. The gene product can be the product of a gene wherein disruption of an upstream gene by the present vector resulted in overexpression of the downstream gene, and the overexpression of the downstream gene

demonstrated a transformed phenotype. The composition can be, for example, an inhibitor, such as a small molecule inhibitor, of the COX 2 enzyme.

Diagnostic or therapeutic agents of the present invention can be administered to a subject or an animal model by any of many standard means for administering therapeutics or diagnostics to that selected site or standard for administering that type of functional entity. For example, an agent can be administered orally, parenterally (e.g., intravenously), by intramuscular injection, by intraperitoneal injection, topically, transdermally, or the like. Agents can be administered, *e.g.*, as a complex with cationic liposomes, or encapsulated in anionic liposomes. Compositions can include various amounts of the selected agent in combination with a pharmaceutically acceptable carrier and, in addition, if desired, may include other medicinal agents, pharmaceutical agents, carriers, adjuvants, diluents, etc. Parental administration, if used, is generally characterized by injection. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to injection, or as emulsions. Depending upon the mode of administration, the agent can be optimized to avoid degradation in the subject, such as by encapsulation, etc.

Dosages will depend upon the mode of administration, the disease or condition to be treated, and the individual subject's condition, but will be that dosage typical for and used in administration of antiviral or anticancer agents. Dosages will also depend upon the composition being administered, *e.g.*, a protein or a nucleic acid. Such dosages are known in the art. Furthermore, the dosage can be adjusted according to the typical dosage for the specific disease or condition to be treated. Furthermore, viral titers in culture cells of the target cell type can be used to optimize the dosage for the target cells *in vivo*, and transformation from varying dosages achieved in culture cells of the same type as the target cell type can be monitored. Often a single dose can be sufficient; however, the dose can be repeated if desirable. The dosage should not be so large as to cause adverse side effects. Generally, the dosage will vary with the age, condition, sex and extent of the disease in the patient and can be determined by one of skill in the art. The dosage can also be adjusted by the individual physician in the event of any complication.

For administration to a cell in a subject, the composition, once in the subject, will of course adjust to the subject's body temperature. For *ex vivo* administration, the composition can be administered by any standard methods that would maintain viability of the cells, such as by adding it to culture medium (appropriate for the target cells) and

adding this medium directly to the cells. As is known in the art, any medium used in this method can be aqueous and non-toxic so as not to render the cells non-viable. In addition, it can contain standard nutrients for maintaining viability of cells, if desired. For *in vivo* administration, the complex can be added to, for example, a blood sample or a tissue sample from the patient, or to a pharmaceutically acceptable carrier, e.g., saline and buffered saline, and administered by any of several means known in the art. Examples of administration include parenteral administration, e.g., by intravenous injection including regional perfusion through a blood vessel supplying the tissues(s) or organ(s) having the target cell(s), or by inhalation of an aerosol, subcutaneous or intramuscular injection, topical administration such as to skin wounds and lesions, direct transfection into, e.g., bone marrow cells prepared for transplantation and subsequent transplantation into the subject, and direct transfection into an organ that is subsequently transplanted into the subject. Further administration methods include oral administration, particularly when the composition is encapsulated, or rectal administration, particularly when the composition is in suppository form. A pharmaceutically acceptable carrier includes any material that is not biologically or otherwise undesirable, i.e., the material may be administered to an individual along with the selected complex without causing any undesirable biological effects or interacting in a deleterious manner with any of the other components of the pharmaceutical composition in which it is contained.

Specifically, if a particular cell type *in vivo* is to be targeted, for example, by regional perfusion of an organ or tumor, cells from the target tissue can be biopsied and optimal dosages for import of the complex into that tissue can be determined *in vitro*, as described herein and as known in the art, to optimize the *in vivo* dosage, including concentration and time length. Alternatively, cultured cells of the same cell type can also be used to optimize the dosage for the target cells *in vivo*.

For either *ex vivo* or *in vivo* use, the complex can be administered at any effective concentration. An effective concentration is that amount that results in reduction, inhibition or prevention of the viral infection or in reduction or inhibition of the transformed phenotype of the cells.

A nucleic acid can be administered in any of several means, which can be selected according to the vector utilized, the organ or tissue, if any, to be targeted, and the characteristics of the subject. The nucleic acids, if desired in a pharmaceutically acceptable carrier such as physiological saline, can be administered systemically, such as

intravenously, intraarterially, orally, parenterally, subcutaneously. The nucleic acids can also be administered by direct injection into an organ or by injection into the blood vessel supplying a target tissue. For an infection of cells of the lungs or trachea, it can be administered intratracheally. The nucleic acids can additionally be administered topically, transdermally, etc.

The nucleic acid or protein can be administered in a composition. For example, the composition can comprise other medicinal agents, pharmaceutical agents, carriers, adjuvants, diluents, etc. Furthermore, the composition can comprise, in addition to the vector, lipids such as liposomes, such as cationic liposomes (e.g., DOTMA, DOPE, DC-cholesterol) or anionic liposomes. Liposomes can further comprise proteins to facilitate targeting a particular cell, if desired. Administration of a composition comprising a vector and a cationic liposome can be administered to the blood afferent to a target organ or inhaled into the respiratory tract to target cells of the respiratory tract. Regarding liposomes, see, e.g., Brigham et al. *Am. J. Resp. Cell. Mol. Biol.* 1:95-100 (1989); Felgner et al. *Proc. Natl. Acad. Sci USA* 84:7413-7417 (1987); U.S. Pat. No.4,897,355.

For a viral vector comprising a nucleic acid, the composition can comprise a pharmaceutically acceptable carrier such as phosphate buffered saline or saline. The viral vector can be selected according to the target cell, as known in the art. For example, adenoviral vectors, in particular replication-deficient adenoviral vectors, can be utilized to target any of a number of cells, because of its broad host range. Many other viral vectors are available, and their target cells are known.

Throughout this application, various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

EXAMPLES

Selective elimination of virally infected cells from a cell culture

Rat intestinal cell line-1 cells (RIE-1 cells) were standardly grown in Dulbecco's modified Eagle's medium, high glucose, supplemented with 10% fetal bovine serum. To

begin the experiment, cells persistently infected with reovirus were grown to near confluence, then serum was removed from the growth medium by removing the medium, washing the cells in PBS, and returning to the flask medium not supplemented with serum. Typically, the serum content was reduced to 1% or less. The cells are starved for serum for several days, or as long as about a month, to bring them to quiescence or growth arrest. Media containing 10% serum is then added to the quiescent cells to stimulate growth of the cells. Surviving cells are found to not be persistently infected cells by immunohistochemical techniques used to establish whether cells contain any infectious virus (sensitivity to 1 infectious virus per ml of homogenized cells).

Cellular Genomic DNA Isolation

Gene Trap Libraries: The libraries are generated by infecting the RIE-1 cells with a retrovirus vector (U3 gene-trap) at a ratio of less than one retrovirus for every ten cells. When a U3 gene trap retrovirus integrates within an actively transcribed gene, the neomycin resistance gene that the U3 gene trap retrovirus encodes is also transcribed, thus conferring resistance to the cell to the antibiotic neomycin. Cells with gene trap events are able to survive exposure to neomycin while cells without a gene trap event die. The various cells that survive neomycin selection are then propagated as a library of gene trap events. Such libraries can be generated with any retrovirus vector that has the properties of expressing a reporter gene from a transcriptionally active cellular promoter that tags the gene for later identification.

Reovirus selection: Reovirus infection is typically lethal to RIE-1 cells but can result in the development of persistently infected cells. These cells continue to grow while producing infective reovirus particles. For the identification of gene trap events that confer reovirus resistance to cells, the persistently infected cells must be eliminated or they will be scored as false positives. We have found that RIE-1 cells persistently infected with reovirus are very poorly tolerant to serum starvation, passaging and plating at low density. Thus, we have developed protocols for the screening of the RIE-1 gene trap libraries that select against both reovirus sensitive cells and cells that are persistently infected with reovirus.

1. RIE-1 library cells are grown to near confluence and then the serum is removed from the media. The cells are starved for serum for several days to bring them to quiescent or growth arrest.

2. The library cells are infected with reovirus at a titer of greater than ten reovirus per cell and the serum starvation is continued for several more days.
3. The infected cells are passaged, (a process in which they are exposed to serum for three to six hours) and then starved for serum for several more days.
4. The surviving cells are then allowed to grow in the presence of serum until visible colonies develop at which point they are cloned by limiting dilution.

MEDIA: DULBECCO'S MODIFIED EAGLE'S MEDIUM, HIGH GLUCOSE (DME/HIGH) Hyclone Laboratories cat. no. SH30003.02.

NEOMYCIN: The antibiotic used to select against the cells that did not have a U3 gene trap retrovirus, e.g. GENETICIN, from Sigma. [cat. no. G9516].

RAT INTESTINAL CELL LINE-1 CELLS (RIE-1 CELLS): These cells are from the laboratory of Dr. Ray Dubois (VAMC). They are typically cultured in Dulbecco's Modified Eagle's Medium supplemented with 10% fetal calf serum.

REOVIRUS: Laboratory strains of either serotype 1 or serotype 3 are used. They were originally obtained from the laboratories of Bernard N. Fields (deceased). These viruses have been described in detail.

RETROVIRUS: The U3 gene trap retrovirus used here were developed by Dr. Earl Ruley (VAMC) and the libraries were produced using a general protocol suggested by him.

SERUM: FETAL BOVINE SERUM Hyclone Laboratories cat. no. A-1115-L.

Identification Tags for Isolated Nucleic Acids

Genomic sequences, tagged with a vector, such as the U3 gene trap vector, are given a number corresponding to the genomic library of mutant cells from which the sequence was isolated., and a letter indicating a unique member of the library. More than one sequence with the same number and letter indicates multiple, unique sequences obtained from the genome surrounding the vector insert that "tagged" the gene. Such genomic sequences are obtained using vector-based primers, from which sequencing occurs 3' to 5' or 5' to 3'. In the former case, to recover the orientation of the gene into which the vector inserted, the sequence derived from the vector primer must be reversed and complemented. Such reverse complement sequences are designated "rE". In the case of genome sequencing from a primer that occurs 5' to 3' (i.e. the primer is at the 3' end of the vector), no changes are needed, since the derived sequence is the sequence as it appears

in the gene disrupted. Such sequences are designated "B4". Homologies indicated below each genomic sequence are in the positive direction, unless explicitly noted to be on the negative strand. As an example, SEQ ID NO. 27 comprises a nucleic acid sequence encoding a novel polypeptide on the positive strand, while the negative strand encodes ferritin.

SEQ ID NO:	Lab Designation
1	32-3-2#1E/-rE
2	L191B2E#1-RE
3	L191B2E#3+-rE
4	21-5-9E-RE
homology to: emb/AL021154/HS15005 human DNA sequence	
5	14A14E-rE
6	4cx-b4
7	5a-b4
8	6BSA12-B4
9	X7B/B4
10	x27b4f_1
11	12C#A-rE
12	10-3b(5/2/96)/-rE
13	10_4B_4-rE
14	6BE60-rE
homology to: alpha-trophomyosin	
15	19D3E-rE
16	L19D16E-rE
17	2b_rE
18	14_24_#6-rE
19	7A7'-rE
homology to: annexin II/dynein I	
20	L12cx#6-rE
homology to: gb:X51760 human zinc finger protein ZFP-36	
21	L12cx#11-rE

22 19D5E-rE
homology to: 6-pyruvoyl-tetrahydropterin synthase (gb/M77850/RAT6PTHS)

23 12_3b#7-rE

24 12_3B#8-RE
homology to: gb/AA871174/vq32a08.r1 Barskad bowel MPLRBg Mus musculus cDNA clone 10959265'

25 9B27-2-E
homology to: RAT LOCUS RNU53922 04-MAY-1996; Rattus norvegicus DnaJ-like protein (RDJ1) mRNA, complete Cds, ACCESSION U53922 (on negative strand)

26 x15-rE

27 X11-rE
homology to: ferritin H (on the negative strand)

28 X20-rE
homology to: LOCUS RATGL5A Rat NICER element (GL5-14)5' long terminal repeat, Acc.No. M59028 M33535N1D

29 X4-rE

30 14A7E-rE
homology to: MMSMAD7 3681 bp mRNA ROD 31-JUL-1998 DEFINITION Mus musculus mRNA for Mad-related protein Smad7 ,149 bases

31 14A13E-rE

32 14_7#2E-rE

homology to: N-acetylglucosaminyltransferase I

33 12CX#6-rE
homology to: gb|AA522204|AA522204 vf98g09_r1 Soares mouse mammary gland NbMMG Mus musculus cDNA clone 851872; also 5' similar to gb X51760 zinc finger protein ZFP-36 (HUMAN), gb L20450 Mus musculus DNA-binding protein mRNA, complete cds (MOUSE); Length = 442, 925 bases (shares homology with SEQ ID NO:20)

34 12C_2B#9E-rE

35 12CX#11E-rE

36 x5-rE

37 8C5_11-rE

38 191E2E-rE

39 19_7AE-rE

40 19_9BE-rE

homology to: LOCUS HS347M6 56583 bp DNA PRI 14-JAN-1998 Human DNA sequence from PAC 347M6 on chromosome Xq22, CSTF2 (Cleavage Stimulation Factor, CF-1, Polyadenylation Factor) 64 kD subunit gene

41 191E9E-rE

42 191E8E-rE

43 14C_2E/-rE

homology to: gb/H31084/EST104778 Rattus sp. cDNA - 5' end similar to signal recognition particle subunit(19kDa) (on negative strand)

44 14H1E-rE

45 14G3E-rE

46 14G_2E-rE

47 6_3_6_2E/-rE

homology to: Rattus norvegicus cis-golgi gp130 (on negative strand); and a HUMAN EST (on positive strand) AI127398; qb70g11.x1 Soares fetal heart NbHH19W Homo sapiens cDNA clone (1705508 3' mRNA sequence)

48 14H4E/-rE

49 18A_8_4E-rE

50 18A_8_1E-rE

51 SCB2_19E-rE

52 L197B3E-rE

53 L195C5E-rE

homology to: H. pylori and C.jeuni

54 21_5_7E-rE

homology to: id3 gene; emb|AL021154|HS150O5 Human DNA sequence from clone 150O5; HTGS phase 1 [Homo sapiens]; containing the E2F2 gene for transcription factor E2F-2 and the ID3 gene for Inhibitor of DNA binding 3 (dominant negative helix-loop-helix protein), 1R2, Length = 133667, 971 bases

55 L195B1E-rE

homology to: vK72b07.s1 Knowles Solter mouse 2 cell Mus musculus cDNA clone 960181 5'

56 L194c4E-rE

57 L193A1E#A-rE

58 L192A3E-rE

59 L1739E-rE

60 L192B3E#13-rE
contains sequence identical to: insulin growth factorII/mannose-6-phosphate receptor

61 3 2 4 rE
located in the same region of the genome as calcyclin, but the gene is "read" in the opposite direction

62 36 7 1 a-rE

63 36 5 1 4 a-rE

64 34 25 5a-rE
rat satellite DNA (RATRSSID 93 bp, ROD 12-MAR-1984)

65 34 24-126/rE
homology to:
HSU49928 (3096 bp mRNA) PRI 06-APR-1998, Homo sapiens TAK1 binding protein (TAB1) mRNA, complete cds, ACCESSION U49928 NID g1401125, and
HS333H23 (142274 bp DNA) HTG 17-JUL-1998 Human DNA sequence

66 34 23-1/rE

67 36 5 2-6/rE

68 36 5 2-196/rE

69 34 23-3/rE
homology to: gb|L16546|RATAP1X Rat P-glycoprotein (mdr1b) gene

70 34 25 23-rE

71 36 5 2-196/rE

72 31 3 9/rE
homology to: AA798638 568 bp mRNA EST 10-FEB-1998, vw34b06.r1 Soares mouse mammary gland NbMMG Mus musculus cDNA clone1245683 5, mRNA sequence, 824 bases.

73 31 3 6-2-rE

74 31 3 17-rE

75 31 3 5-rE
homology to: AF046001 2347 bp mRNA PRI 19-FEB-1998, Homo sapiens zinc finger transcription factor (ZNF207) mRNA, complete Cds, 833 bases.

76 31 3 15#1/rE

77 24 3 5#1/rE

78 31 4 4#1/rE

79 31 3 19#2/rE

80 31 4 5#1/rE

81 24 9 3#2/rE

82 L24_26_1-BL

homology to: AI045472 396 bp mRNA EST 06-JUL-1998, UI-R-C1-jz-h-09-0-UI.s2 UI-R-C1 Rattus norvegicus cDNA cloneUI-R-C1-jz-h-09-0-UI 3', mRNA sequence.

83	L24_26_1-B4
84	L22_5A1/rE
85	L24_3_2B/rE
86	L24 4-2/rE
87	L24 5-2/rE
88	L24 5-3/rE
89	(15-)L28AP/rE
90	L24 26-10/rE

homology to: LOCUS R06687 403 bp mRNA EST 03-APR-1995; yf10a10.r1 Soares fetal liver spleen 1NFLS Homo sapiens cDNA clone 126426 5'

91	L24 26-2A/rE
92	L24 26-2B/rE

homology to: gb|AA590026|AA590026 vm22g03.r1 Knowles Solter mouse blastocyst B1 Mus musculus cDNA clone 990964 , 459 bases, 139A; and Rattus norvegicus Eker rat-associated intracisternal-A particle element

93	14 7#2E-rE

homology to: N-acetylglucosaminyltransferase I; this sequence shares homology with SEQ ID NO:32.

94	x18
95	31_3_9-rE
96	31_3_6_2-rE
97	31_3_17-rE
98	31_3_15#1-rE
99	24_3_5#1-rE
100	31_4_4#1-rE
101	31_3_19#2-rE
102	31_4_5#1-rE
103	24_9_3#2-rE
104	14XD#12E-rE
105	70A-rE
106	31-3-4-rE
107	3_6_9-NeoG-rE

108 31_4_2-rE

109 3_2_13-rE
homology to: calcyclin

110 3_2_4-E
homology to: pistlre-alpha 1 (with homology to calcyclin on negative strand)

111 L25-10/-rE
homology to: calcyclin

112 L24-4-3/-rE

113 L24-9-1-rE
rat id sequence

114 17-L25-27#7-rE
homology to: calcyclin

115 L21C1E-rE
homology to: calcyclin

116 L24-5-3BE-rE.
homology to:
LOCUS H32572 310 bp mRNA EST 08-SEP-1995 EST107805 Rat PC-12 cells, untreated Rattus sp cDNA 5' end, ACCESSION H32572, and
LOCUS AA858747 470 bp mRNA EST 10-MAR-1998 UI-R-A0-bb-e-01-0-UI.s1 UI-R-A0 Rattus norvegicus cDNA clone UI-R-A0-bb-e-01-0-UI, 3' similar to gb|AA473081|AA473081 vd44b07-r1 Barstead MPLRB1 Mus musculus cDNA clone 803413 5' mRNA sequence

117 L24-4-2BE-rE
homology to: LOCUS MMU51002 6495 bp DNA ROD 16-JAN-1997 Mus musculus Dlx-2 gene, complete cds, ACCESSION U51002 NID g1477589

118 17-3-3B-B4

119 L24-26-3/-rE
homology to: RNU23776, DNA ROD 10-AUG-1995, Rattus norvegicus Eker rat-associated intracisternal-A particle element

120 12_2B#2-rE

121 05-17-3-3He-1-T7

122 21_5_8E-rE
homology to: emb|AL021154|HS150O5 Human DNA sequence from clone 150O5; 1p36_13-36_22, contains the E2F2 gene for transcription factor E2F-2 and the ID3 gene for Inhibitor of DNA binding 3(dominant negative helix-loop-helix protein, 1R2, Length = 133667, 971 bases

123 X18H-t7

124	18A_8_4E-rE
125	L24-5-2BE-rE
126	L24-4-2AE-rE
127	L24-10-1BE-rE

Genes Necessary for Viral Infection

Some of the isolated sequences dislcosed here comprise sequence encoding the following proteins: tristetraprolin (human ZFP-36), 6-pyruvoyltetrahydropterin synthase, a eukaryotic DnaJ-like protein, ID3 (inhibitor of DNA binding 3), N-acetylglucosaminyltransferase I (mGAT-1), cleavage stimulation factor (CSTF2), TAK1 binding protein, human zinc transcription factor ZPF207, Dlx2, Smad7 (Mad-related protein), and P-glycoprotein (mdr1b).

Isolation of cellular genes that suppress a malignant phenotype

We have utilized a gene-trap method of selecting cell lines that have a transformed phenotype (are potentially tumor cells) from a population of cells (RIE-1 parentals) that are not transformed. The parental cell line, RIE-1 cells, does not have the capacity to grow in soft agar or to produce tumors in mice. Following gene-trapping, cells were screened for their capacity to grow in soft agar. These cells were cloned and genomic sequences were obtained 5' or 3' of the retrovirus vector, i.e. SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:36 or SEQ ID NO:94; sequences designated with an "x" in the clone name). All of the cell lines behave as if they are tumor cell lines, as they also induce tumors in mice.

Of the cell lines, two are associated with the enhanced expression of the prostaglandin synthetase gene II or COX 2. It has been shown that disruption of gene function by retroviral targeting of an upstream gene has lead to increased expression of a downstream gene product, COX 2. When a small molecule inhibitor of COX 2 enzyme was added, reversion of the transformed phenotype occurred. The COX 2 gene has been found to be increased in pre-malignant adenomas in humans and overexpressed in human colon cancer. Inhibitors of COX 2 expression also arrests the growth of the tumor. One of the cell lines, x18 (SEQ ID NO:94), has disrupted a gene that is now represented in the EST (dbest) database, but the gene is not known (not present in GenBank).

Each of the genes from which the provided nucleotide sequences is isolated (and all clones designated with an "x") represents a tumor suppressor gene. The mechanism by which the disrupted genes may suppress a transformed phenotype is at present unknown. However, each one represents a tumor suppressor gene that is potentially unique, as none of the genomic sequences correspond to a known gene. The capacity to select quickly tumor suppressor genes may provide unique targets in the process of treating or preventing (potential for diagnostic testing) cancer.

Isolation of entire genomic genes

An isolated nucleic acid of this invention (whose sequence is set forth in any of SEQ ID NO:1 through SEQ ID NO:127), or a smaller fragment thereof, is labeled by a detectable label and utilized as a probe to screen a rat genomic library (lambda phage or yeast artificial chromosome vector library) under high stringency conditions, *i.e.*, high salt and high temperatures to create hybridization and wash temperature 5-20°C. Clones are isolated and sequenced by standard Sanger dideoxynucleotide sequencing methods. Once the entire sequence of the new clone is determined, it is aligned with the probe sequence and its orientation relative to the probe sequence determined. A second and third probe is designed using sequences from either end of the combined genomic sequence, respectively. These probes are used to screen the library, isolate new clones, which are sequenced. These sequences are aligned with the previously obtained sequences and new probes designed corresponding to sequences at either end and the entire process repeated until the entire gene is isolated and mapped. When one end of the sequence cannot isolate any new clone, a new library can be screened. The complete sequence includes regulatory regions at the 5' end and a polyadenylation signal at the 3' end.

Isolation of cDNAs

An isolated nucleic acid (whose sequence is set forth in any of SEQ ID NO:1 through SEQ ID NO:127), or a smaller fragment thereof, or additional fragments obtained from the genomic library, that contain open reading frames, is labeled by a detectable label and utilized as a probe to screen a portions of the present fragments, to screen a cDNA library. A rat cDNA library obtains rat cDNA; a human cDNA library obtains a human cDNA. Repeated screens can be utilized as described above to obtain the complete coding sequence of the gene

from several clones if necessary. The isolates can then be sequenced to determine the nucleotide sequence by standard means such as dideoxynucleotide sequencing methods.

Serum survival factor isolation and characterization

The lack of tolerance to serum starvation is due to the acquired dependence of the persistently infected cells for a serum factor (survival factor) that is present in serum. The serum survival factor for persistently infected cells has a molecular weight between 50 and 100 kD and resists inactivation in low pH (pH2) and chloroform extraction. It is inactivated by boiling for 5 minutes [once fractionated from whole serum (50 to 100 kD fraction)], and in low ionic strength solution [10 to 50 mM].

The factor was isolated from serum by size fraction using centriprep molecular cut-off filters with excluding sizes of 30 and 100 kd (Millipore and Amnicon), and dialysis tubing with a molecular exclusion of 50 kd. Polyacrylamide gel electrophoresis and silver staining was used to determine that all of the resulting material was between 50 and 100 kd, confirming the validity of the initial isolation. Further purification was performed on using ion exchange chromatography, and heparin sulfate adsorption columns, followed by HPLC. Activity was determined following adjusting the pH of the serum fraction (30 to 100 kd fraction) to different pH conditions using HCl and readjusting the pH to pH 7.4 prior to assessment of biologic activity. Low ionic strength sensitivity was determined by dialyzing the fraction containing activity into low ionic strength solution for various lengths of time and readjusting ionic strength to physiologic conditions prior to determining biologic activity by dialyzing the fraction against the media. The biologic activity was maintained in the aqueous solution following chloroform extraction, indicating the factor is not a lipid. The biologic activity was lost after the 30 to 100 kd fraction was placed in a 100°C water bath for 5 minutes.

Isolated nucleic acids

Tagged genomic DNAS isolated were sequenced by standard methods using Sanger dideoxynucleotide sequencing. The sequences were run through computer databanks in a homology search. These genes can be therapy targets particularly because disruption of one or both alleles results in a viable cell.

What is claimed:

1. An isolated nucleic acid comprising a nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127.

2. A nucleic acid comprising at least 20 consecutive nucleotides of a nucleotide sequence of claim 1.

3. A nucleic acid comprising at least 30 consecutive nucleotides of a nucleotide sequence of claim 1.

4. A nucleic acid comprising at least 40 consecutive nucleotides of a nucleotide sequence of claim 1.

5. An isolated nucleic acid encoding the protein encoded by the gene comprising the nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5,

SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127, or a homolog thereof.

6. A host cell containing the nucleic acid of claim 1 or 5.

7. A nucleic acid comprising a nucleic acid that selectively hybridizes under stringent conditions with the nucleic acid of claim 1 or 5.

8. A nucleic acid having a region within an exon wherein the region has at least 50 % homology with a nucleic acid of claim 1 or 5.

9. A nucleic acid having a region within an exon wherein the region has at least 60 % homology with a nucleic acid of claim 1 or 5.

10. A nucleic acid having a region within an exon wherein the region has at least 70 % homology with a nucleic acid of claim 1 or 5.

11. A nucleic acid having a region within an exon wherein the region has at least 80 % homology with a nucleic acid of claim 1 or 5.

12. A nucleic acid having a region within an exon wherein the region has at least 90 % homology with a nucleic acid of claim 1 or 5.

13. A nucleic acid having a region within an exon wherein the region has at least 95 % homology with a nucleic acid of claim 1 or 5.

14. A polypeptide comprising the amino acid sequence encoded by the nucleic acid of claims 1 or 5.

15. A nucleic acid comprising a regulatory region of a gene comprising the nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127, or a homolog thereof.

16. A construct comprising a regulatory region of claim 15, wherein the regulatory region is functionally linked to a reporter gene.

17. A method of reducing or inhibiting a viral infection in a subject, comprising administering to the subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82; SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127 or a homolog thereof, thereby treating the viral infection.

18. The method of claim 17, wherein the gene is selected from a nucleic acid encoding a gene product from the group consisting or, or the gene product is selected from the group

consisting of: tristetraprolin (human ZFP-36), 6-pyruvoyltetrahydropterin synthase, a eukaryotic DnaJ-like protein, ID3 (inhibitor of DNA binding 3), N-acetylglucosaminyltransferase I (mGAT-1), cleavage stimulation factor (CSTF2), TAK1 binding protein, human zinc transcription factor ZPF207, Dlx2, Smad7 (Mad-related protein), and P-glycoprotein (mdr1b).

19. The method of claim 17, wherein the subject is a human.

20. A method of reducing or inhibiting a viral infection in a subject comprising mutating *ex vivo* in a selected cell an endogenous gene comprising the nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82; SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127 or a homolog thereof, to a mutated gene

incapable of producing a functional gene product of the gene or to a mutated gene producing a reduced amount of a functional gene product of the gene, and placing the cell in the subject, thereby reducing viral infection of cells in the subject.

21. The method of claim 20, wherein the cell is a hematopoietic cell.

22. The method of claim 20, wherein the subject is a human.

23. The method of claim 20, wherein the cell is from the subject.

24. A method of screening a compound for effectiveness in treating or preventing a viral infection, comprising administering the compound to a cell containing a cellular gene comprising the nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82; SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117,

SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127, or a homolog thereof, and functionally encoding a gene product necessary for reproduction of the virus in the cell but not necessary for survival of the cell and detecting the level and/or activity of the gene product produced, a decrease or elimination of the gene product and/or gene product activity indicating a compound effective for treating or preventing the viral infection.

25. A method of screening a compound for reducing or inhibiting a viral infection, comprising administering the compound to a cell containing the construct of claim 16 and detecting the level of the reporter gene product produced, a decrease or elimination of the reporter gene product indicating a compound for reducing or inhibiting the viral infection.

26. A method of screening a compound for effectiveness in treating or preventing a viral infection comprising contacting the compound with the gene product of a cellular gene comprising nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82; SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID

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27. A method of suppressing a malignant phenotype in a cell in a subject, comprising administering to the subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid set forth in SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:36 or SEQ ID NO:94, or a homolog thereof, thereby suppressing a malignant phenotype.

28. A method of screening a compound for effectiveness in treating a viral infection, comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product whose overexpression inhibits reproduction of the virus but does not prevent survival of the cell and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for treating the viral infection.

29. A method of screening for a compound that can suppress a malignant phenotype in a cell comprising administering the compound to a cell containing a nucleic acid functionally encoding a gene product encoded by a gene comprising the nucleic acid set forth in SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:36 or SEQ ID NO:94, or a homolog thereof, and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for suppressing the malignant phenotype.

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

(X) Original () Supplemental () Substitute () PCT

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am an original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled **"MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION"**, which is described and claimed in the specification

(check one) [ ] which is attached hereto, or
[X] in International Application No. PCT/US98/21276, filed October 8, 1998, and as amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose all information known by me to be material to the patentability of the claims of this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a) - (d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate relating to this subject matter having a filing date before that of the application on which priority is claimed:

PRIOR FOREIGN APPLICATIONS: (ENTER BELOW IF APPLICABLE)			PRIORITY CLAIMED (MARK APPROPRIATE BOX BELOW)	
APP. NUMBER	COUNTRY	DAY/MONTH/YEAR FILED	YES	NO
PCT/US98/21276	International	08/10/98	X	

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States

provisional application(s) listed below.

APPLICATION NUMBER	FILING DATE
60/062,021	October 10, 1997

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose all information known by me to be material to the patentability of the claims of this application as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION SERIAL NO.	FILING DATE	STATUS (MARK APPROPRIATE COLUMN BELOW)		
		PATENTED	PENDING	ABANDONED

I hereby appoint the following attorneys and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1-00
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Inventor's signature: Date: 3-28-00

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Citizenship: United States of America

2-00
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Inventor's signature: Date: 3/28/00

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3-00

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SEQUENCE LISTING

<110> Rubin, Donald H.
Organ, Edward L.
DuBois, Raymond N.

<120> Mammalian Genes Involved in Viral
Infection and Tumor Suppression

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aaccncgggg nctcntgttt tattttaaaa aaaaagagtc ncatgtntat ttctctnatg 180
tgaaaatcnc attcanagtt ntggggtttc ccntgaggag anatagagtt tcacactctt 240
ctctccgagg ggtcntcnca tgtntctccc caatgtgngn ggnacacaca tgnggccccn 300
aggggggtgng ctctctctgc ncagggcncc ccccaanang tagaganaca ntgtggtgtt 360
tcacaacaca attcncgaga nattntgttc cncantggnn gtctnagntc ncatgttgtg 420
gngacangtt agnncncccc atnttcnccc ccctttcaca ctgccccnag agagagaaan 480
tctnggcccc ctctanannt ntttttaaat cnccccnnac cacaggtntt cccagggtat 540
gngacntcnc cnnccccncn aaagatntgc nc 572

<210> 8
<211> 906
<212> DNA
<213> Rattus norvegicus

<400> 8
tgggagtctc tctcatatgg cgcnttcncc aaaggggngt ctctntccng agncgcanac 60
gcgagaanac tctgtnnant ngtctccccc cncnccnaca gngtganant caaaacctct 120
agagcccccc agaaancccc tntctcaaan aaagagaaag agaagancga gnagnagaga 180
gananagaga gagagagtgt gganctntnt cctcngancc ccannnanan ngtgnggcnc 240
actcncnngt gnngngnacc ccnggggatt tncgcgtgtc cccttgngct ctgtntanga 300
gananatatg tntagtctct ctntcgcccc ctccgntgtc acgtgtgcgg ggcccnngag 360
acacagacac ntctctcang gggaacacat anngactcnc acntgtgttt atattcnccc 420
ctcccnctca cacanacaca cacacagnag atattnngct actctctctc tgtcacaggg 480
gtacanattt antctnggcc anacccctct cngaagngng ggcanngtaa accccgcccc 540
ctctcngaga angngaggg c gntttacntt cccngtggcg tgtncgngcc cccgagactc 600
cccttngnac ccccctntna accctctntt tgaacncaac ncaccntccc cnttttctcg 660
gggnnggncc ngcnccccnct ctcncaaaaa aaattnnaan ttngtcccct nccccnttnt 720
ttcnggnana aaccgtgtcc gggggggggan nactcttttt tgnccttaaa atcaantttt 780
ttccccttttt ccnggggacc cccgnnttcc tttttaaaaa aaaanaaccc tttctccctt 840
ttaaaagnac ccnttttttc naaaaccgtt ccgnatttaa ttcctaaatt cccttccccn 900
nccccgg 906

<210> 9
<211> 914
<212> DNA
<213> Rattus norvegicus

<400> 9
gggatgngcc ctcagatcaa tacacccctc nggggngtc tctctctatc tcccncagna 60
gactcccatc tctntntntn cccccaganc tggngaacgg ngtgtggnga nccntntctg 120
ttctcnantc tctaaaagng cnaaaagcgc ananacacgn gcctctctat anatctcacg 180

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tgtcccnngn nctctcngac ccctnntctg tntgagagac accctntctc aaaatatagt    240
gtacacgngc tttgnggctc tcccctttc tctccactnt tgagngngaa acgcggngtt    300
ntctctgaga tgtaganagn gtcccctnct cnatatatgt gttncccact ccnnagggng    360
tctcataaaa atcncntntc tcaacaccac cncctcnacc ccccncacga gaacacntcn    420
ccaccncnan gacacaaana naaggngtnn anaaccccan aaaaactnng ntntcngntt    480
tacacacaca cacacncacn ctcncncaca cccccacnna aatgggagaa aaaacagaga    540
ggngtgggtg ttngnntcaa caccntntta cctctctgnt gnnanttgag aaaatatttc    600
tntncttacc cctctcccct ctctgtgtgt ngannatatc ngntctagat gtcctnaccc    660
tccccaaacc tttctcnggn agagacntct ctntnttttt cccccncttc catttgaaan    720
anangagaag gnccaaaaag gngggngtct tctcgggaat ncnccctttt ggccccccaa    780
cctgggtttt tttcccctt cctttaatn antttttcna nacaaanctt tnngngtttn    840
ggaaaangcc tttnnctgnn nntttttcc cttcccttt tnnangggnt tcccccccc       900
ccngaatttt tttt                                                      914

      <210> 10
      <211> 400
      <212> DNA
      <213> Rattus norvegicus

      <400> 10
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acagtttatg aatattatta catatttcac aagactttat attgttataa tatgcctcat    120
gtgagatata tgtgattctg tggtggtgtt ctcagagggg gtttgggtta ttggggataa    180
tagtttgccc ctcgcggggt ctatatttat atatgtgaca caatatatta gagagatttt    240
tggttatata tatttccctt cgcgggggtg gagatttatc acagggggag agcttttccc    300
ttgttagcaa aagtccctgg tctcgtcccc catctcccaa aaaaaaaaaa atgtgaaaaa    360
aaaaaaaaaa agggcccctc ttgagtgatg tccccttctt                          400

      <210> 11
      <211> 880
      <212> DNA
      <213> Rattus norvegicus

      <400> 11
acccaatctt nanggtggca gtgnggnnga tcttaacggt ttttnagaaa aaaaantnct     60
tcgctcncac ccccaagcct cccnttctta ncagcttttt tatangaaaa aagatgataa    120
cgaaatttta aaaaccgtcg ttagaggaaa tgaaggttca gccgaccatt acctganagt    180
aatgaaggtn ttccggaggg ttgccttcca atcccagatg gatttgagtt tcaggatcaa    240
ttcagttacc gntgaccatc caccnncctc cngtataatc attngatgag gatgaatggt    300
gagtgagtga tgatgatgat gatgatgatg aagggatgag aagnacacta tgataacaag    360
tgtctcagtc cacattaagg tttgcctgna aattagtgca taagccatgg gagacaaatt    420
cttttcnnac acaattaata gtntcttant ccttcccatc ttctctgccc cattctgttt    480
tccaccacag gtctgcagcg ggctacagct tccagtctcc aagcaaatac cagaactgga    540
ggagaaaatt ccagtccagt gagtcatggg caggggggagg ggtggggtaa gggcagtggc    600
gctcattcct nacatggtgt cttctcttgc ctagcctggg atctgagggc aagagaacct    660
gtaagcttga tttgatttcc actgctgact ggagtcactg ccaagggatt tgggacttct    720
ccatctctct ctctaacctg aaatccttag gattctatta tttcaccgga ccagagctgt    780
agcagagatg agctccaagt ttgaaatgag aaaggggaaa ttgagagcta tgagctaggn    840
gcgaaagncc ccacaaagnn tttggcaagt agaaaagncg                          880

      <210> 12
      <211> 909
      <212> DNA
      <213> Rattus norvegicus

      <400> 12
cgngagnngg cagggannna ggngggagcn ngagaggaga aggagaaggn nnggnaggng     60
nngngagnaa cgggcgggan cnnnngacga gagaangggn aggggancga agngcggngg    120
nagacggtgc nngggggggga ggggcaggag nggnagagag gcangagngg agnggggaca   180
agcnnaaanc gaggaggnan gangngangg nnggngngnc gaaggcgcnn aagnnggtcg    240
gngagcggna gnggnnaaac tggggaacga gacagacggc cccnncggng gcangnggga    300
gagnnncgcc agngagagna gncagnanca gancangga gggggggan ncacnggcgg      360
gagggncgan gacggnnngn annggnnaga ggcannnnnc gccnanagng ngaagngagg    420
cangagtgnc gcnngagnag acaggcccgc gcnccggggg cagacnnngg ncaccaccga    480
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gggtgggngg ggcncggaga naagaccaga ggnnngaggg cganggcnng ggtnngcccg 540
ggccncccna aaaaaanncc gaaaaaaaan aaggggcgcn gcngggcngg ggaggagcgc 600
ntnncgtang tngantgacg gaggccngna atngggccgn gccanncnag ggcgnagagg 660
cccaagngcg gnaggngnaa gnanagancc ngnnggtngg gagnganagn gcnnggnncc 720
naccccccngn gttganggcn cccacgncgg ngcaggccgn nnaaagngag tccccnaaaa 780
nntcgnggtn tnacancgnc ccggggncgc cgcngngtcc cgncacacng gannncggag 840
anngcctnnt ntctncacan ggngccanac nngntgctat gcaaaagggg cgnacttcna 900
gaaaaagnc 909

<210> 13
<211> 927
<212> DNA
<213> Rattus norvegicus

<400> 13
cctttattcg gaggcaggga nnncttgtcc gggaangtta aacgtttttt aaaagggggn 60
ncccnggggg gggggnttnt ccagggaant aaaanggtgn gttgggggn aaaaatttat 120
tttnaaaaag ggcgnccnat ataaangacn ttcgggggg tttgaanagg gccggaancn 180
tcgacgggtt tccgggnggg ganaaggana agggnacgca cgggatttct tnccctttt 240
tngcaaattg cngcaggana ccaccgggtg gggnggtttt gttttccgtn aagaaagcgg 300
gngtggaaaa acanggataa acgggaagan ggggttattt nggttagnaa ttgnttccag 360
nggngccagg aaattggcct gtccaaaatt cttttcccng cttttaagac aggcaggtat 420
tatttggcag caggttatta cnataggnaa gtaaataaca atgggtaagt gcctggcaca 480
ggccagggta agtagggcat gtatggaatg ttaaacatta cccttcatcc tgagaaanaa 540
aanacaagna anaaaggctg gtctcacata tcccaaagct ttatcttcnt aggtgcccca 600
tggtgaacgt taagccaagc ntatgantca caagggacga catgggcagg ntagggtaca 660
gaatcagtgn tcagagactc caggggcacc cctgattccc tttgctgtca cacagacact 720
gctccaggga caaccctccg gatgtgagta tatgacttcc tgatggtgac gctgccgtga 780
tgggacactc ntcgtggtag cacacattcc tcagtcagct tctgagcntc agggtcccag 840
cagagcacag tggcaangac tttcattctt nttggncttt cccaggggc gtncccaaat 900
ggaagatttg gcaagntaag gaagntc 927

<210> 14
<211> 848
<212> DNA
<213> Rattus norvegicus

<400> 14
ttttccaagt aaancanggg anttcggtan aagaangttt aaanaagngt ccaggcancn 60
gaaattttcg nggntttggt taacgangca accagggggg ggtttcaang ggtcttctaa 120
tnatttnaan gggngtagtt tctggtnggt tcattccttn aaaaaaaaac aaaacaaaac 180
aaaccgnagc ttctgcattg gccaccngtt gnggcaccaa cccttnangc attgcccttt 240
ccttcctgcc gtgtcgggng gcgctaagcn gcccttgtca ccttccattt ntngatcatt 300
ttccatgtcc ttgcacttct gcttccactt cntgttggta gacgagctgt atgntcagaa 360
antgaagtac aaggccatca gcgaggagct ggaccacgct ctcaacgata tgacttccat 420
gtaaatgttc atgcaccctg cctgcttgca ccctcaccnt catgcttgtg tgatgacctc 480
accgtggctc ccccannann aaaananatc catgtctgca ccttttgttg gctttcttgc 540
ataacctagg ataggttatc ttttccacgt tgcactaaca aggccacgcg cattcggtcc 600
gtgaaaccac ctcggcatcc ttttatntca tagaggcaaa tntagcttgt ttctgccgag 660
agatgacctg gactccgaat gggctctgag tatntccttt taaaacctta aaccagantc 720
aagtaaagtt aggaagccat gaggcagtgg tgcaggaagt taggaagaaa naccgggttg 780
ttggtttcct gggnctgggg tgagggacca ttgatagacc tttacgaaan ganccgcang 840
atagaaaa 848

<210> 15
<211> 896
<212> DNA
<213> Rattus norvegicus

<400> 15
agagaaaaag gaaanannga aagaaagagg agnaaaaana aagaggnggn aanaaagaan 60
agangnanaa agaananant nngagattac gaantcgggg agagngaaag gaaacaaagn 120
nggnggnaaa gagnnanttn tttcaagggt ccgnaacaaa aagttgagng angattccna 180
acaagggntn nccacccaan ctgntaaagg gangatttgg ncaaacanaa accngtattg 240

```
gggagttaaa aagagtcacc aaatagggaa aaaaagttng ggggagggnn aacnacnggg     300
taaaggttcc aggaccagag ngttcagnac caagtttcag tattcaggag gacagagttc     360
aggatcnntt tggaacattg gggtttgggt agcntggnaa cacgaaccct tttgttcata     420
aaaaggaagg gaaaagaaag ggnngaagag tnttcccaga tgnattntga gcagagaatg     480
cccgaccccc cgaatacgta gttccaaaat gggattgnac ctgtttcacc tcaaatttca     540
ntcntccttc tngtggacag acgcagggat ggggtcgggg aaggggngaa gctggtgcgt     600
gttctgtggt tgccggtgga tgntctgcag ctgtntaccc caccgaaaac gaatggatgg     660
gatgtcactc ccaggcagta gggggcgcac gcgcattgtg ttntagagag anttccccag     720
cctccccngg aannacaaca cgttntcttc ttcttaaggt ggtggtgggg gggggggga      780
agacctattg ctttccgaga ggatcggacc aaacagcaga ttntgctcaa ggcccttgaa     840
ccctgntatc tcactaaaca tctgagatac tgacattaca gatacggata tcgtgg         896
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<210> 16
<211> 858
<212> DNA
<213> Rattus norvegicus

<400> 16

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gccaatcaag ttncggttaa attttggaaa ngnggcgaat gcnntgtctt gnggattttg      60
gagggnggaa ngtnggtnaa agagttttaa tgttcttggg atcgcaanta ttttcctggt     120
tcgcgncttg tacattatga gggttgataa cngctgtttt tngattttgg ttaacanggg     180
ngggngcntt tttnggntga cctntagtnc ntcngngccg ggcattttgg ntaccttttt     240
atttttngaa gtncagggat gttgtgtact gggaatattc cttagaagtg accatgattt     300
tatattttat taaatatata cttagattca ntctttgcct aagcctggat gttgttggtn     360
tttgtttttg ttttgttgtt nggagagttn tcattttccc aagctggctt tgaacattca     420
cttccacaca aacatgtcca cacacggcca aaggtgtatg cacagatatg gacataacac     480
acacagagaa gaatnacaaa caaacaaaca aaatatttcn gacagaaaca antaaataca     540
tccagaaggt agaatattct acaaggcatc aaatctgttc taaagaaaaa gttataataa     600
agaaaaacat tgaaaggcag gtgaaggaga ttgaaggcca taggggccac aaaaaggttt     660
aaacagcaaa gcaccaacgt agatatccgg aacgtgctaa atatggcaca cacaggatat     720
ccgggaacga tgagtcagcc agcggcacat ataaccaacg atgtaatctg ttatgtaact     780
atgaatcatc cctggcagag tgccaccttt gtgtgatttt tgtataaata tgcccctgag     840
accagaagcc attgcctt                                                   858
```

<210> 17
<211> 551
<212> DNA
<213> Rattus norvegicus

<400> 17

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ttntctgtac cccttctca aaaaaagtgg ctggtgnctt ttctcngaag agaatcctca      60
ccnccncana anaaatatct ctctcccccc cttgttgntt gtcncccnnc ccaaaantgt     120
gngatctntc tctctgtgca cgaganattt tagaggggga tatccccggg gtgtngccng     180
tgtctntcct ctcgcgaata tctttangag nctctctctc tcganccccc agngtaggnn     240
gagngganaa catttttntg tggnggcccc ccacaananc acnaacaana tattttcgag     300
aancncatgn ganaatcggg gggggggggg ccngtgttna cacnatancc ngggngatna     360
nanagacacn nnatatntct gggntgtgna aanataanac aagancanac atgnggagan     420
natgtgagan tgtgcacacc ctgttgtgac atgtgaggtg gggggctgat gatncctncc     480
ttctacgtnn tntcttctcc tccncantga tagacnccac ctgctggagt gnctagctan     540
ctggggtcgg t                                                          551
```

<210> 18
<211> 888
<212> DNA
<213> Rattus norvegicus

<400> 18

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gttaaatatg aaaaagtggg ggtgacaggg ggtgataccc tttgcgccgg gctatggatt      60
tttggcaccg ataagatttt caggtgacat ggaaggtggt tggggatggg ggaaagtttt     120
gaggggccaa aaggataagg aggatgattg attggtttgg gagcagtact tggaaagagt     180
gtgtttgatc ggtaaacaac cacgtgtagt gtgtttttgt tgcagcagag ataagtgaga     240
aaaagatttc aggagatctt gatttttttc gggtcgagct atgttggggg atgtgagggt     300
acaattcaca agatttgttc acagggagtt ctaggaggtg gtcccattag ccggtagggg     360
ggttttctca ataaatgggt tcagtcaggt gtttgcctag atctttcatt agttcctccc     420
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ttcaaaggga ttttgaagga gtgctttgtc ctgtggagca attgactcaa tcaataaact    480
taagtaatct cccggattac tgttgatgcg ttcccagaga ggtcccccgt agttaccagt    540
gaatcacaat ttcctaacca tatgattttt gttaatctca ccacataaac ccacaattct    600
cgcgtccttt gtgatggttt caaagtctgg aatattttttt cctccatccc tcctttcctt    660
cctcctttta tccctccctt cctttttttcc tttcacagga tctcattatg cagcccagtc    720
aggccttaaa cttgtgatcc tcctgtctca gcctcctagg tgttaagatg acccaaatgt    780
aaaccatgtc cagttacttc ctcctaatcc catcttcaga tatcctttaa gaccaaatta    840
aatattaact gaaagacccc accagtaggt ttggcaagct agcaaaga                 888
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<210> 19
<211> 867
<212> DNA
<213> Rattus norvegicus

<400> 19

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ctttttctaa attttttaac gggggaaatc aaacggcaaa aaagaggggg gaccacctca     60
atcacccaca gtggaaaatt ggtgggtatc aatcaggtgt tattaggggg ggaggaatgt    120
tggggaacaa aaaaaaaatt ttaaaaattt ccaggggggt tttgaaggca ggtgatttaa    180
aaaccgcccg tcagttaagg gggttttatt ttttttttaat aaaaaataaa attaggattc    240
tggaatagaa tttttaattc agggatcctt atttttaatg tttccagggt aaaagggaga    300
tattcttatc aggtttctgg aaaaagtttg cttggtttcc tttggcagga gagaggttta    360
aaaaagactt catttgaact ttttgatcat tgtgtaaaac tttttttttt gaacaaaaca    420
ataaaatgta aaaagatata gatcttaggt tttttaaaag acaaacatat aaaatattaa    480
aacagattgt ctgtcccatg caaatgactg actgaccttg taacagctcc acagagtgtg    540
taaaaacaaa aaaaagcccc ctgagagcct tgagccatca ggttaagtct catttattaa    600
tattttcaag gccacaggag acactctgtt cccttcattt agggaggtgc tgaggcagcc    660
atgttttccc agcagtgggg gttgggcaga gccactccag attggcttgg aggggtgtgt    720
agctctcagt ctgcccggac ttggatggtt tattttctta aacgaaaaca cctgcctgag    780
aaagagccct tttcacgggg tggccaagtc ccagcccgcc ctgggagcca aggtcaagtc    840
ttagcttagc gttctaagga cacagat                                        867
```

<210> 20
<211> 897
<212> DNA
<213> Rattus norvegicus

<400> 20

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aaagggnanc aaaaccntaa nggggagggg nggggaaatg gccaaaantt ggggttaaaa     60
aaagttagga tntggttgga tccnacccac aaggaatttg ttnttaattt tttaaaggna    120
aatttgggca cttcnattgg gaaggttaaa acccaggcaa gtgntaccgg gntatgcaag    180
tgaaacntga ttctggnggt ggagggaagg atantganat gtgagtgagt gcagttgagt    240
gaggacttgt gagnacaggt catgcccacc aaagggagga gcaagggtgg gcagtggtag    300
gtggtgtgtg gttcctttct gggggntggg cggggagaca gatgagaacg ntattggagg    360
acaggnacaa gtgtactgaa atgcaaatcc ctgtagatct ggaaaaggtc tggnttcagg    420
cttgatgctt gggccggcaa ctgtgnacct tccctgnacg ttcagccccc ccacccttac    480
ggaagttttc gtcactgaag actagtggct aatcagagtc ttcaatggac ctgccaatca    540
gaaaggaagg cgggntnttc cgggtgcnta ggtgtaggat tcgctcagta gttaagcagt    600
cttaactggt tctggctgct gtgctntctg tcctgccgtt ggattntctg aggcatgttc    660
aggcaagctc caaagttgcg acatggtgag cacaggggca gggggggcgg gcggacgggc    720
aggggactga gcagtgggag ctggtgtggt gggtctttcc cggggctgag ttggaatccg    780
cggctacccg tgaggtctta gccactcact agacccagcg gcagtttctg aataactttc    840
nttgtagggg ttggnactcn gnaaagactt ccacnaaggn cttggcaagt agaaagg       897
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<210> 21
<211> 435
<212> DNA
<213> Rattus norvegicus

<400> 21

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gattccagag agaggagtga actggcagat aaggcagtca gcataatggc ttagatacca     60
tgtgctttcg ctcactatgc acccatgaca caagatcaca gggtacaggc ctggaccatg    120
gcagagtata cactggttgg gtaaatgaag aggagagaca gagtgggaag tcggcttagt    180
ggatatggac ttcaaatttg atgaacaagc aattcaaatg agtatcgtgg gcttgantgg    240
tatgaagacc cgtttgcaaa gcagtggtca taagagagaa aagagagaga gagagagaga    300
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gagagagaga gagagagnaa gagagagagn gtgtgttgtt gttgttgttg ttgttgttta 360
ttggttnata acaanatnta cctttgggcn ctttngaaag actntncaca aaggagcttg 420
ncaagctaga aaggt 435

<210> 22
<211> 894
<212> DNA
<213> Rattus norvegicus

<400> 22
gaaaaaaaaa aaannataat tttaattttt cccccatttn aagggaaatn ggaaattaaa 60
natnggtttt nagcccaatg gaaattaaaa ttaagaaggt tgttttccaa aaacctttcc 120
ctagaggana accggccnat aggnggggn agnatggaag gattttccag agaggaatca 180
gtttggngag agaatttgat aaggagttcc ttggaaccaa ccnggagggg gttttggttt 240
nngggattna tcangatggt tgtccttggg aagcataagg ntggtttatt attttggtta 300
aaggggatga agtaccntgt gttgcacttg gtagcccaat gtcctgtcat tgtgctttgg 360
atgtaggcag ctttgaaggg atttntcctg agaggatctt ccggatcaga gtatatcgcc 420
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gcagtgcggt gacacacgtg ggcacacccc acctgtgcag ccggtggctc gcgntgaagg 600
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gaccaaagac ccacaagnta cgggttccgg tttccgggac ngaggccagc ccggttcccc 720
cgcggntgcg cagtgcaaan tcggccttcc ccgccggaag tactcctggg agcggtttcg 780
gcgcgtggca cttttcggtc cacctggagg caacactggc gccntttcct gtttcagtct 840
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<210> 23
<211> 594
<212> DNA
<213> Rattus norvegicus

<400> 23
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nagagtaatt tcaaaagccc cagntttgtg gaatcanttt ttgaanatat gaaaaggccc 180
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gtttntggca gaaacagaac agccccgttg gcacggacag tgtccactgt ttatctataa 300
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gggagtcaga gaggtcggaa caatgaggcg gaaaccaaaa ntntgaaaca cgcccacctg 420
aacaggacga aagggtgggg cttggtccac ccagaaggaa acctcgaact ccacntttca 480
aggtatccgc tccgggttag cagccccggc caaacgcccc tgctggcttc taacccaacc 540
agctacgaaa gcaggctnga ccactagctg ncctcgactt gaaagttccc acaa 594

<210> 24
<211> 586
<212> DNA
<213> Rattus norvegicus

<400> 24
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tccaaataga tgtatttcaa aagccccagc tttgtggatc agtttttgca ntatatgaaa 180
aaggccttan tgnttcggga ttattaaggc ccgctgagga cactgttagg gcgcntcaag 240
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ctgtttatct ataaatcttt tcaagcagat cttgcagcca actaggtaca agagtcggat 360
ggggatgggg ggcggggagt cagagaggtc ggaacaatga ggcggaaacc aaaantntga 420
aacacgccca cctgaacagg angaaagggt ggggcttggt ccacccagaa ggaaacctcg 480
aactccacnt tcaaggtatc cgctccgggt tagcagcccg ccaaacgccc tgctggnttc 540
tacccaacca gctacgaaag caggcngacc actagctgac ctcgac 586

<210> 25
<211> 909
<212> DNA
<213> Rattus norvegicus

<400> 25
gggggttgn aaattgagaa gcccnccttt cntctttgtt gtgaanacat ttnccntncn 60
gggggatccc tnggttccgg aagggccgcc ttagttnttc ttttcctcca cctatgaaag 120
gggngggagc cgattaaaag aagggnggag cagngaggga agcggagctt cgcccgtttt 180
ccgnacccctt aaccctgctt gttcgggggg ggagngtgcc accnacccgg gngnggtggc 240
acggagatnt gagggggagg gatggtttgc cntggccgct ngtgggtggg cgggcaggcg 300
ccggcattcc cggcaccttc ngaagacnga gccgggttca gggacnnaca ntccccgcca 360
agngggacca accgcttcgg gtgggttccc cggttgtntg gtgcccaggc cgnacgccgn 420
gacngaggga gacccaagga cntagantca ccggtgagcg ggccggcgcc ggagagcgga 480
aagaggagcg tagcacagcg cagntcggcc agacgttgtt cttntaccac ccaccgagcg 540
tttaaaaaaa anaaaaaaan cccgcggcag cggacttttt ttgtagcgga gcccgggcgn 600
gtcacttgcc ggaagtcccg cccntcgttt ctgccaccgc ccntcggtta cctgggcaac 660
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ttcccgatcc tngtagaatn ttntagaggc tttttcttta tgcgaggtac cagagggcgg 780
aagtcttgag gtggagaggt catgtcccag agccgtaagc cggggacgag tgctntcagg 840
cnntgtgcan ttgggatcct nnggnccacc ntgagggtcn tcacaaanga agcngncnag 900
taaaggagt 909

<210> 26
<211> 576
<212> DNA
<213> Rattus norvegicus

<400> 26
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gtngggggct ccaagggggn nggggaganc tnaagntcnt caanntagag agggggaagc 120
tccccactct acatctgttg tcggagcacc cccccaccca gagggcgctg tcagtcatag 180
actagagacc tcccctcaag tgnctcnatc cttccaatag acgagccctc ttgacgcctt 240
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ggagagcgcg cgacatcgcg tgtgaanngc gacctgtctc cgcggagaat gggagtgtct 480
gtgtgcagat gtcatagtga gaaaccaccg ataagggtga tagggtaaaa gatacttaaa 540
gggctatgaa gaaagtgggg aagggaggag gggaga 576

<210> 27
<211> 853
<212> DNA
<213> Rattus norvegicus

<400> 27
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tcctttgaan acccngaaaa attcatttnc agaggggttg gaagggggag ccgaaaagaa 180
accccaacna cttcgcaagt aacaangggc cnaagggagn cagccgcacc tttttccnc 240
cccgcccaaa ggccagccgc attcaccatg aacagataga ngtaggaggc aaacaattcc 300
agttaatntg gcggttgatg gcancttcgg attcttggtg gtatttctgg cgnatttgcg 360
agggagacgc ggtgttcatg atggcggctg ggngaggcgc ggaggcgacg ctggagcggc 420
ggagcgacga agttgcaaag gntcaggttc aaagcgnccg gcggggtcgg aggggtcgag 480
caccggttcc gttcaagcac tgttgaagca ggaaaccgcg gngantctgg gcgagaangt 540
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ccaatcagcg cggtgggccg cccagccccg cttnttcctg taggcgtgtt gcccaagcca 660
gcagtgcgtg ggcggggagg agcctgtgtg attgtgaggc gantcttggg gttatgagct 720
gntgcaagag cggtgcctgg caacaagcgg gacgtttntg tggcccgggg cggacgtagt 780
tggaaccagc cgtactacag aggcattctg ggtcccagag agtatcgata aggttgattt 840
ttaagtccca ccg 853

<210> 28
<211> 825
<212> DNA
<213> Rattus norvegicus

<400> 28
ggntttncagg ggnaccccccc ccccncttnn antttgtcca cgnaanattn nngccnnnna 60

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aggangggggn ngggaagttt nagggcaang aaaagggaaa agtttngttt ggacaaacct    120
tgaaaggggn tttatcgcaa nacnccgggg gggggttttt ttgaaagaga aggggaaaag    180
attcggaanc ctgatttttt tggnttgagt naagnggggg angggnngna aaaattaaan    240
ggattccngn gggggngact agtantttag gggggagaaa agggttttat aaggncccat    300
aaagttcagc ggaaagccgg ntccggggaa gaccacccat gngttttaat tagagtgcaa    360
cgggttgaag agcccaggaa gcccaganac tagggtgagt caccgngaaa ntaacagacc    420
ataaaaggaa ggatgcagaa cagaccaggg tacnantcac aggccacttg gcaggaagag    480
atagccccca gccccngaat ncagagcccc aacctgccaa tgnggtagnt ataccttatt    540
acttcatcat gtgaatagcc aatcatatgt gaacatgtnt atgtgcttcg tttgaatcca    600
ccaatcccng taantatgat ntgttctgna cgcccgnttn tgttccccaa tccntataaa    660
agccccatgc tggagctgct gggcgcgcaa gtcntccgaa gagactgtgt gcccgcaggt    720
acctgtgttt tccaataaac cctcttgctg attgcatccg agtggactcg gctcggtcat    780
tgggcgcttg ggactcctcc tgagggaaag tcctctctgg ggtct                    825
```

<210> 29
<211> 861
<212> DNA
<213> Rattus norvegicus

<400> 29

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anngaaacat ncccnncnnn ttnatccttt nggaaaaggg cancccaaag gnnnggaacg     60
gatngaanaa ttctttcaaa aagaganatc gganggnnat cgnnnnggtt ttcaagtccc    120
cccngagnan naaaattgag tcagtngggg gnaaccgacg nananaggaa caggtttccc    180
gggagtcctt gggtntcngt tcgacccccg gaaaccgaac tnncgcnttt ncctttggga    240
gnggggattt ntaaaggnna ncgggngtat ttccattcgg ntagttgttn gttcaagggg    300
gntgccggac ggaccccctt tnagccagac ngngnnccta tccgnaaaan tgttggggtc    360
caacccggta agacagattt ntcgccantg ccagcagcca ntggtaacag gattagcaga    420
gagaggtatg tagacngtgn acagattaag gaagtggtgg cgtaagnacg gacacattag    480
naggacagta tgnggtatct gcnctcggtt gaagccagtt accttnggat aanganntgg    540
tagntttnga tcccggcaga caaaccaccg ttggnagcgg tggntccttt gnntgnaagc    600
agcagantan gcgcagaaaa aaaggatctc gagaagatcc tangatatnt tgttcggggt    660
cagacgctna annggtntgg natnntganc ggntgaccat agagcacagt antgnngatt    720
gcagtccgcc ccnaggacga naggagacca ggggcccang ctgnagtaac naatcaacta    780
ccctnacnag atgnancaga gagagagagn accgtatant nantgnaaga gaggtcccgg    840
tttcnagttc ccagnacgga a                                              861
```

<210> 30
<211> 149
<212> DNA
<213> Rattus norvegicus

<400> 30

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attngaggag atccggttac taaggatata gaagaaaaaa ataaatcgtg tgcctgcctt     60
ttttttttta attgcctgct tctccccacc cccaaattaa gttgcttagc aagggggaaa    120
gaggcttttc ctcccttcag taggtcagc                                      149
```

<210> 31
<211> 857
<212> DNA
<213> Rattus norvegicus

<400> 31

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gatctggtct tgcccnggan ganntcnntn ccgggggggn taaaaaagaa ttgntggngn     60
tgacnagggg gganaccccn taccgngggn cnancggaan tnttggncac cgnaaaaaat    120
ttccaggngn acangaacgg gtgcggnggg antaggggga aangtttgga gtgngccaaa    180
acggaaaagn agacgnttgt anggggttggg aaccagnacc ntggaaagan tgnagttctn    240
atcngcaaca accaccggag gtagggggtt ttttgtngca gcacagatan gcgcagaaaa    300
aaggatttca ggagatcctt tgatttttat tcgggtanga cgttcangtn gnggggattg    360
ggagcggana accatttnna cacaggattn tatgaactat ggtcanttgc tttgttgtcc    420
angtcgttgt gggattgctg tttttagtag ctgcaaacgg ttcgttttnt gctatctttg    480
ttnngataaa tcagccccgg gcagangana ttcgaaagtt ccctttagga gcttatttan    540
acgggctcaa ngccaccggt ttcgtttttn taggcacgtt ctgcgcattt tttttttttn    600
gnatntttgg atcgcgtttc gtgggatctt aaaaaccgtt ttctgtgatt ggcacgcaag    660
aaanactcat gagctggtcc ctgttgtgtc tctcaggacc aatcaaanac ccatttccaa    720
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```
cggctttata atgtctggtt ctgtttgcac aggaagcgaa gtcacggctt gcacccgtga    780
agtctgggga ggttcagagc tgggaactgc ccagaggaag gggttcgggg ctacagccat    840
caatcttcca gttgttt                                                  857
```

<210> 32
<211> 1630
<212> DNA
<213> Rattus norvegicus

<400> 32

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cccccccccc ccccaaaaan aanaattacc nttttaccat tgnggttccc ngtccntgat     60
aaatttttaa ccnncntttt tccttaaaaa ancgnatcct gangggattt ccgttnaatg    120
gnnttaannc ttttngngaa tgttnacccc aatnttcccc tnaattttga gtnngataat    180
tgcttanagg catttggaaa tttaacggnc acctgaggtt gattggttgn tattnaacgg    240
acttngatnn gaggaaggcc cccaanattt tgttccattc cttntaagtt tgggacttgg    300
aaatcccgtt gtttagatct tgaccgtaat caggagtcag cgtagaggag gccccggaag    360
gagggcccag cgcggattcg cccgcggcag ggcggggacc aacagagggc cntcggggat    420
aggggagcgc cgcccgccn tcccggggaa ggacacattg cttgttagca ggaagccagc    480
cagacccgga ggaggccgct ccagcgttgg tgttgccggt ccggggctag cctgatccgg    540
gcagggtgag ttgagacgat cgggtgagct tgggccgggg acgccagcgt cttcagtcct    600
ggggattgtc ccaggagggc aaggagcttg gaggagggag gccgcacagc taggggagtc    660
aggtctgagt cccgagtgtg ctctaaagcc ggggcggtga gagtggcggc ccgcccgggg    720
ccgcgcagcg ngcagtctcc cccgcgtggg aagtggtaac ttaacgcaca gccacaggat    780
tcccggcctt tagctgctgg agggagggtg gcttctcccg gaggagtctg ttgtgaaact    840
cggttggagg gcaccgtggg tgcgggcaag ggagagatgg ggtcgccctg aagaagtggg    900
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gggctcccaa gaggtataga gtccccccatt ttacaaaatg tggttcagtg ggactgtggc   1140
ccacccagtc gtgtatccat ggaagagtgg cttttatgga gaagttcatt ttccttaacc   1200
ttaaaaactg taaaggatct tgtgcttgag aatattgttg gccagcttta tagtcttcat   1260
ttataaaact atttagacta gagtgttata gattataggt cttcaagttt ccagtcacca   1320
gtccttggct ttttagtatg gaaatcacca gtaatggcaa tataacatcc ctgcttctgt   1380
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actttatacg taggacatca gggtattgac attctcatcc taaagtcagt ttgtctgttt   1500
ccagaggagg aactgaagca gtggttcttt aagtaactga ctcagggctt tcctgcctgg   1560
cgcgcctgcc aggcatagtg tagcattgta ctgcatcttc tttgaccagt ttccccaggt   1620
gaagagcctg                                                          1630
```

<210> 33
<211> 883
<212> DNA
<213> Rattus norvegicus

<400> 33

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ggaatttgtt anaattttnn taatggaaat ngggcacttc aattgggang ataaaacccc    180
aggaagtgat accngggtta tcaagtnaaa cntgattctt ggngnngagg gaaaggatat    240
tgaatttgag tgagtgcagg tgaagtgaga cttgggagna caggtcatgc ccacccaagg    300
gaggagcaag ggntgggcag tgtaggtggt gnggtggtcc ttcctggggt gggcggggag    360
acagatgaga acgttattgg aggacaggca caagtgttac tgaaatgcaa atccctgtag    420
atntggaaaa gttctggntt caggcttgat gcttgggccg gcaactgtgn actttccctg    480
tacgttcagc ccccccaccc ttacggaagt tntcgtcact gagantagtg gctaatcaga    540
gtcttcaatg gacctgccaa tcagaaagga aggcgggctt ttccgggtgc ntaggtgtag    600
gattcgctca gtagttaagc agtcttaact ggtttntggct gctgtgctct ctgtcctgcc   660
gttggattnt ntgaggcatg ttcaggcaag ctccaaagtt gcgacatggt gagcacaggg    720
gcaggggggg cgggcggacg ggcaggggac tgagcagtgg gagctggtgt ggtgggtctt    780
tcccggggct gagttggaat ccgcggctac ccgtgaggtc ttagccactc actagaccca    840
gcggcagttt ctgaataact ttccttgtag ggctgcaac tct                      883
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<210> 34
<211> 913
<212> DNA

<213> Rattus norvegicus

<400> 34
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ggttttntcc nagggggggа gaccccnttn nccgcgggcc tttcgnaatt ttttggtcca 180
ccngtnaaag attttcccat ggcgcaccat gtacgggttg cgaggngtat taggcggnaa 240
cggtttttna gtgggcctaa tacggnanat aggaggacga tttgtnttgg tttgtngagc 300
cagtaccttn gnaaagagtt gtagttttga tccggcaacc aaccacngtt gtagcgnggt 360
tttttgttga agcagcanta acgcgcagaa aaaaggatnt caggagatcc tttgattttt 420
cttcgggttc ngacgttatg ttgtgtggat tgtgagcgga taacaatttc acacagattc 480
cgatngtagt ccaatttgtt aaagacagga tatntttccc ttcaaagaaa acagaaaaat 540
acagaaacgt taattttcaa atctcnaatc tttcnttctc tcttcnntca ttcattcntt 600
cnttctttct tctttctttc tntctttctn nagaggaggc atgctagggt aacagtagct 660
cattttaaaa tctggcacct ggaattaatt tagggacaaa acacctttat gcaaaaaaaa 720
gtttatgttt ttccatggaa cacagtaaaa tcaaaattaa aagaatataa caaaggcttt 780
ggtgatttgg taggattttt tttttcctgg aggggaaaac agatgacttg gaaagtgtta 840
ggaacatatc aagccccagg gaaagaaaaa cgtttgattg gtattaatta aaacactgct 900
aatatattct aat 913

<210> 35
<211> 320
<212> DNA
<213> Rattus norvegicus

<400> 35
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aatttgatga acaagcaatt caaatgagta tcgtgggctt gactggtatg aagacccgtt 180
tgcaaagcag tgntcataag agagaaaaga gagagagaga gagagagaga gagagagaga 240
gagaaagaga gagagtgtgt gttgttgttg ttgttgttgt tgtttattgg tttataacaa 300
gatntacntt tggtaacttt 320

<210> 36
<211> 389
<212> DNA
<213> Rattus norvegicus

<400> 36
ggggggggngc naaaagggtc tttcttttna naaaaatcnn gganggaggc cncnanacgg 60
ctnttanann tnttcngggt gtncctcncc gntgtgggga atganatntc gntctcgaca 120
tcaggggatt ggagattntc tgngctcncc nctcacnacc cagaagaagc gcacagagan 180
cagagtanca catcatacac acctnttcag ctacagagcg antnctctan aaggggactc 240
gggggganaac acaaccctcc tcctcttctg actgngagng ccgcntgtag gntctgtcta 300
cccancaagn cttgtgcagn ntgngaacct ctctntgggg tagagtgtgt tgngggagca 360
gggcgtantg ttccaggnct agnctttca 389

<210> 37
<211> 882
<212> DNA
<213> Rattus norvegicus

<400> 37
agnaacgcgg ncggnggnnc tcncccngcg gagcnggncc ncccccnngn ncccagaana 60
gnagcgctcg gngannnccc acgngnagac nnnggctgcc ccncgngncc anggcnttnn 120
nccnnccccc cgnatccggn ncncccccccc ctccctnggg gngcgggggt cccngngccg 180
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gccgcggcca tcggaacncn cctagcagng cgtcntgcta ggcnggnnna cgggnatccg 360
caanccccncc cttngtaccg ggacagccgn gggnccgtat gggctgngcg ntnggccgta 420
gccanntncc tttngaaang acncggnagc tnttcatccg cctcacaaac cncngggncn 480
gngggggctn tntcntgngc cgcccgccgc gtgngcgcan aaaaaaaaaa aanncggccn 540
tccnccccctc ttttggccng ggtnccccgc ncaccccgtg ccgagtnccn nnccccccac 600
aacctcacac cgatcccngt gggttcccnn ngggagtcgc ncgngcnnag cnggnttctc 660

cccatnncgc gnngcttnag cgngccnnnn cacngtttgt nngngnntgc ctccccttcn 720
tccttgaggc aaaagcccgn acngtntctg tggaccacnn tgctgaggng ctgggcgccn 780
cgntctctct ctctctcnct ctctctctct ctctatctct ctttctctct ctggggcccc 840
tcccttgntg nngccanaag nnngcnnacc cgtaaagtaa gt 882

<210> 38
<211> 975
<212> DNA
<213> Rattus norvegicus

<400> 38
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tttagcgngg ttctcnagtt natggtaacc nagtacttaa ttggcncnct tgataaatgc 120
tngatcctna naatttcaac aaccgcagga ccatttttga acttggcggn ngtttaccct 180
tnatgnnctt tccnnaaaat ggcttccttt gncatcnaat agtgntgccc ctaacccctn 240
ggttccggag gatgcatnng tggntgtgng tttgnccttg agcatgcngt tccgtnacgg 300
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ttcgggatta tatnagttta tgtctgnttt tcataaaatc acttgtggat ttggctttaa 420
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cttgtatact aaagtgacat gtcnttntng acactaacaa tcacaaatta ggagtaccaa 540
tcaactttga gaaaatttaa aagatgcccc atctcttgta tcagcaagta ttcagccagg 600
atttaattct ttatgtaaaa attagcaagc atttctatnt cattcacgtg caaatttttct 660
ttgattgtta attaagattg aagtgatatg tatggcccaa ataagtctca ctttaaaaaa 720
tatttcttta tgaattatta tccatgaatg tttgatctgt atagctattt tatataagta 780
tatgcaagga ttgctaaaac aatttttgag tgaaaaaaga tcctaggtag aaaatgttta 840
agactaccta taccgtcatt aaaaactcct caccagcatt tactatggtt ggactttcag 900
agatctcaat caactctttc ccacccagtc tactgaaagn ttccacctgt agcggcccaa 960
gcaaactgag atntt 975

<210> 39
<211> 850
<212> DNA
<213> Rattus norvegicus

<400> 39
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ggtttcaaac aatgcttaag ttgtggggag aacnagncag tccgttccng acccngttta 180
tcntaaagga gacggnggtt aaaggttagg gggttngaca gtcctgctgg tgttcaagga 240
ggaggagaca agttgncatc caggngngca ggaanacctg ttaaattcct gaccnaccgg 300
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ggtatcacgg ccccccctngg gtttccattt gcagtttgta ttggaccatg gatcactgct 480
tccttntgcc ggaagttcca gattccaaac tgtgngantc ccatntgcaa ctcccatgtt 540
tgccgntggg acttttntta atatcntggt acccgcttcc catttcccca cccccntgnt 600
cccttcggga ggaatcaccg cccagtgtgt cacttcctgt aggnacttcc aaggntagat 660
gagtgagtgg caggcctcac nttggcccag ttantcagtg cccacagagt agcttttttg 720
agacgntagt aaggtcttag gggaaggaat gtagtcgatc cttctccttg gtggccctca 780
gcactgtgag tagaccccac acatcagggc tgtgtcgtta ggatctctgg gagggttgaa 840
agtttcgagg 850

<210> 40
<211> 889
<212> DNA
<213> Rattus norvegicus

<400> 40
ggggtttcca aaaatttggg gntttggana aaccttcggg gaataaaaca acngnnnaaa 60
attaaggggg gccgggggaa aaaggagatt nattaaancn ccacccgaat tnaaacnccc 120
nccgggaccg naaccgtttt tggccnaaan ncgagaagtg ccttccnggc aaagtagggg 180
accaaaggtn gggggagaga attggggttt gtncagngtt ccggttcnac ggaaggagcc 240
ggttgttggg attgtttcca aggagngngt ttgngaccgg agcacctcng gggngaccat 300
ggggnttgcc tgttagagac cngcgngatg ttttgggttc gnattcgggg agggatttcg 360
ggggcctcag acnggggagg agtcccntgc gttcccnatg ggaccggttg tcgggcgggt 420

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gcagtttcgc tgctgtcctt tggcaatgng cntgggnatt ngtgggcaga ngagattccc     480
cngccccccgc natttccccn gttccagttc ntaggnacca gaggttttcc gcagtgtgat    540
tcagggagnt agantntagc gtctgtnttn tntgcgtttt ccccttcatg attctcagtt     600
atttttttagg agaaaaggtg cgtggaaaca gagcgtccct gttccgtgct gtttctcnta    660
gcccaaaata cagatttaat tctgaagcca tcgacccccca tatccacttc ccgccctctc    720
ataaacgtgt aatatggctt gctttttcct tgtaacgttt catccaacca tagtggtagc     780
ggccacctgg catcttgagg tgggttgcga atgagtgaat gaatgagtga gtgaatgaat     840
gaatgaatga atgaatgaag caagcttcag ggagattttc agagaagtg                889
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<210> 41
<211> 929
<212> DNA
<213> Rattus norvegicus

<400> 41
aatgcccntn aggggnnttt ccccgnattt naaaatgggn tncnngnttc caaagtttcc      60
taaaaatttn cantttccgt ttttaccngg tttatggttt ncagcctact cctgttcgan     120
ttccaaatcg gtttaantgg ncccnccgaa ncnttnttn tttggcagaa ggtgaanttc      180
nttggggccc ttgtttaagg gttttnagcc ttaaattgnt tgntnagnnt ctccntaatt     240
agttcattcc tttgaccatc ttttgnccct ccatcttgta aacanttaag tctattgcat     300
tccactttnc tntcagttnc cgtttnaccc tcctnagcag aacccgnttc tcagctntgg     360
atggttccaa anggtttccc aacctatgct caataccaca ggcagcttgc aggagggaga     420
antggtatgt atttaacagc attttgaccc aaacttttag gagcagagag gactttaccc     480
aggacaggaa ggcaaaagac ttgaatctta aacaaaggat taagaacagg atgtcatctg     540
tgagcctgtc acagtgggtt tgcagagcag gagaacacag acaggattag ctataaagtt     600
gttacattag ttattntatt ggagcataca atacttaaat agttctaggg caagagaaat     660
gaacagaaat gaccttataa gagccagagc tgtagccaca gctttctttg tgcttagttt     720
gctagttcac tctttccagg gcagtctggt ggattacacc aaattgctta gaaaatgcta     780
gctctactgt ccctgtctat tgtcagcttt gcaatgtgca tagtgacagg agttgcctgg     840
gaagcttggg gcttatgttt tgcagatcca ttgtaattaa aaaagaattg taaggagatg     900
gaggcacggg gtgagggtga gggtgagtg                                       929

<210> 42
<211> 943
<212> DNA
<213> Rattus norvegicus

<400> 42
ttggaaaccc caacctggaa aangngtntt nccgggaaat tcaacctgcg ggcnaatggt      60
gtaaaagggc ctaccttggc ttngaaggga atntcctgaa ggnnnaatcc caannttgtg     120
natcccaatt aaggntnaac nggtttaatt tgtnntccnc ntaccnaccn ggtttnccgt     180
tatactaaag ggctaacaat taaatgctca naagggaccc ccaatcctng gcnagaactt     240
gggttaaggn ttccattagg atttgccatc ctntaccgtg atcctgaaca tntnttgaac     300
tgntttgcca aggaacngaa ggttttncct naagntagca cacagcagng accaaggatt     360
ggaacccagc nagtgcttgg aggtaaaaga tcacttccnt ntcccttagt caggancntt     420
agggagtgga ggcatcaccc acacattccc cagtttgnac gtaggtttca gccagcaanc     480
cgtccactaa agctgcctcc aattcaaact ggattgagtg acaagtggct tgggtgtctc     540
tcaaagattt ataggtggca atggccactc ctctgtgtaa ttaccctnta tgcacgtctt     600
tttnttctct cccactccat cccccacccc tctttgtttc ttcntccntt cctntccctc     660
ctgttgactt tttctctccc tgcaaacagt tccaggcacc gnttagcatn tgccactctg     720
gctntagaaa gctttgcttc ccctctgctc cctggctggc tggaactcag cctccggtgt     780
gggcagactg gctcatcctc tgtgtttctc tgagtgtgga ctgctgcctt ccacacagac     840
tctctgaagt caaggagccg caccagcact tcagttgtgg gccataatca agncangact     900
gaaagttgcc acctgtagng gccgcaagca aactgagatn ttg                       943

<210> 43
<211> 867
<212> DNA
<213> Rattus norvegicus

<400> 43
aggaaaccnt tttaaaaaaa aggggggggg gggggggggn ntagnggcaa aaaagatgan      60
accctcaagn cggggggggt taaanaagga atcggattcg ggctttgnac aaataaagga     120
gttttgngng nattttcccc ntggtcgttt tntgnacgat ccacggttga ccgacgacgn     180
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acggaccgac aaccaanacg taaaggggaa ttgtggaggg gttggaagtt tagatgcccc    240
gacccaggac gtgcggccan cttccggaga cccacctttc ttgtnggccg ggnccggcgg    300
cagcgnagcc atttccaccg gatccctata gcnggccagc ctagcaggcn gaacaccagc    360
gggaagttga ntnggacctc ggagagcgcc cgcccttccg gcggaagtnc taattccaaa    420
gcggcccgcg gcngagtttc ccatacaggt tggttccgtc tcggagtgac gtggcttgaa    480
ggacggtctt cgcgcgagaa gagtaccctg cctttcaggt gcgggagtta cntcagcctg    540
ctgcacaccc ggctgtgcgc antcttctgg tgtggccggg acggttcacc cagaggagtc    600
tctgtagttc ggagcaagat gtcggttaaa tctggcagga aaatgccttc tatgctcatn    660
tatatattcc tgcttccctc agcttgcttt cgacttagta aggtaacatt tcagagcggt    720
gcacttagta ctttttggca ctgtgctgta taaatataaa tgttccacac ttaacatctt    780
agatgttata tctaaagata tgcatcttta aacttcgaaa gcgcataccc taaaatttca    840
tatttttgca tacattggtc agctgtg                                        867
```

<210> 44
<211> 303
<212> DNA
<213> Rattus norvegicus

<400> 44

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ggaaatgatt agtccaagaa atatttgagc agaagggagt tagggttttc aaattaggaa     60
agtggaatcc acagagttcc cttgacagag aatataaaaa ggactctggg gtgtcagaat    120
ggtgggcatt aacctgatct tccacttgag ggtaagggaa atgattagtc caagaaatat    180
ttgagcagaa gggagttagg gttttcaaat taggaaagtg gaatccacag agttcccttg    240
acagagaata taaaaaggac tctggggtgt cagaatggtg ggcattaacc tgatcttcca    300
ctt                                                                  303
```

<210> 45
<211> 840
<212> DNA
<213> Rattus norvegicus

<400> 45

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aaaccggnng aanaaaaaan gaaanngang gcnnnaaaaa agttnngaca gaaaaaactt     60
tnggaaaaaa gganggggan aaggcaggng nccnactnaa aanggncttt tcnaagngng    120
anagagntgg naatnagnaa naggacattc ttnnaacctc cnanggnggn nggaannaat    180
ngggattgag cngccaccat tagggangaa gttngaattn nggggcccgn gngagttaaa    240
angattcccn ggttttttaa aacagagaat acctncaggn acagatnaac ccgagattgg    300
ttccctngaa aattnnngan aaagataaan gtaggagcat tcaaagtagn anggtaaaan    360
taatgggaga catagacacc aaaaaaagcc agttcagtgg gccccgaagg ngcattaagg    420
gaggaccagg aaacggcagc anagccacng gcagccgcct gccccnacac cagtnattcc    480
cgcacntaga tccaggcgnt gggggcgggg cggggcgcgc ntgngcagng aagntnngcg    540
gcaacaantt tgcntagacc ggntggaacc ggttagaacc ggccgcgccg gaccggccgc    600
ccgttccgga ttntgcgttc acaaagggag gcgggactca cgacntgngt atcnttgngg    660
tcccaacccc ggcccccnac cccnaccccc nttgtccctg tggcattcgc gttctttccg    720
ccgtctccct cgcgggccgn ttntctgcgc ctggtgatcc tttcgccatg gtcctntgga    780
gaaagaaaaa atctttaatt tnctagggac gtccttttcc tgtagtcgta attgtagaaa    840
```

<210> 46
<211> 893
<212> DNA
<213> Rattus norvegicus

<400> 46

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gagaaggann aggnggggng agngaagana gaggagggaa gaaangaagg tggaganaag     60
tggannaaaa agagggagan ggagggagaa ntaaaganag ganaagagng gggaggaggg    120
gnagnatagg agaggaaaga aagganggan agaagagaaa agaanganga gagaaaggaa    180
agaggaaaga aagaggggag aagaggaaga aanagaggag gggangagag ggaggataag    240
agaggaaaga gggaganagg nttgaaaagg gaaagagaag gagaaaggna gnaggngngg    300
aagagaggna agggagaggg gganaanggt aagggggnaa agaangagaa gtatnggggg    360
aaaggaggag angaaagaag aaagaganga ggaggagagg gagagtgagg aataaagggg    420
agggaaaagg angagaaaga gagagaggga gagggaagaa nagagaagga tagnggggtg    480
gagaaggaga aaggagagaa ggagaaggng agaggagaan tgaagaagga gggagtaaga    540
aaggantgag naggaaagga ganagagagg tagagagaaa anaaagaggg aaanggaggg    600
gaggagggng nanaaggaat agagggngga aanangagag aggggaaang gggaaggaaa    660
```

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ggaggaaaaa aagnagagaa gaagagnaat gggaaggang nagtagnaaa agaaaagnag    720
aggggagagg gggangangg ggganacggg ggggaanaga aaaagtgaag gaggcccccc    780
nacccccccc ccccacacac acacacagcc ttttcgccgg cggaagtgca ggttggtcca    840
ggagcctgtg gtcaatccag tcagtagtgg gcgaggtgta acatctgtgt ccg           893

      <210> 47
      <211> 789
      <212> DNA
      <213> Rattus norvegicus

      <400> 47
taaaananng gnnganannc tnnaaaaaan tntcttngga attnncagga nggaggntaa     60
tngggcgggc ancatcaatg gtanaaattt gggggggnng annaaaatca tnaanncaac    120
cgtttccana gncaaccatt ctgggngncc caaggttnga ngagntccgn tcaaggngaa    180
accttttcaa gaccaattaa ctaggggatn agaggcgggn tggttnntga ggggcgggct    240
gctgagaaga ttcgttgggg gacccaggag tgaaggtttt tnacctgtgt ntntcgggaa    300
ggtcggatnt attatantcc tgctgttgga ggagttcggt ggttcaaggg ccggacccgg    360
agcgtttact ttttnttgnc cgcagccaat ttgttntgct tggtttcttc ngaatcccgg    420
ggcggggagg gggaagcggg gggcccaatc accacgatcc cggcagccac cgcgaaattg    480
ttccggcagn tacgantctt caacaagagc cagagaaggc gggtgcagag nttcattagg    540
acgntcggaa acccggcgtg acttactttn tccaagccca ttggttgatg agaatgatga    600
ctgacaggga ggcgtggtca cgctgtcgcg ggcgggagcg acgggtggag ttaacgacga    660
aagctgcgcg cgcagccatg acccctcaca gccacntatc ggagggaggg gcgggacagc    720
tttagcttgg tgcgtgcgca gccggacgtg aggcagttgg tggtcttcca tcgtcgattt    780
ctggttacc                                                            789

      <210> 48
      <211> 872
      <212> DNA
      <213> Rattus norvegicus

      <400> 48
gggggnggct tttttnggag gcatanatng gggnnngtcc ggnaaacccc attggtcggc     60
cggggaagga aaanggggct ctnaaaatan gttantggga tggngcctta aggggggcc    120
catgngccag gaangcagat tcaaaaatgt tccaagtgga aaaccanggt tggnanaggc    180
cctccnggnc gtnaaggagg agaggagaga tggagtttca ggtgtgtttc ccacccagtg    240
ttcccaggga acacaaaacg gataggtcac cntcaatgna caaggaatta aaagcttggg    300
tgtatnggga ggcctgcttc caaagccacc agaaaatccg gagagccggn ggatcntacn    360
cacccagagg ttcataggga gggcantatt aggggtgtgc ccttgtgaga ggaagtgtgg    420
cacngtgggg ctgggtttga gatntcagat gntcaagcca ggcccattnt ntctctctca    480
gtntctctcg gtctctttct cngtctctnt tcagtctntt cagtctctct cagactctct    540
ctctctctct ctctctctnt ctctctctct ctctctctct ctctcccngc tgcnttcaga    600
tatagacgta gaantctcnt ntatccagca ccatgtctgc ntgcatgctg ccattnttcc    660
caccangacg ataataggct aaacttntga actctaagcc agcctcaatt aaatttntan    720
gagtcaaacc agcctcaatt aaatgttttc atttctatga gtcacagtgg tcatggcatt    780
tctttacagc aatagaaacc ctaactaaga cttgccgaaa cctcaaccac aacttcagcc    840
ctcagaagcc caagagggaa aagaccttga at                                  872

      <210> 49
      <211> 785
      <212> DNA
      <213> Rattus norvegicus

      <400> 49
tcgtaanttt tnatccaccn gtanangatn ttccatgcca ccatgtacgg ttacgaggng     60
tatagcgtgn acngttttgg agtgngctaa aaggaaatgg agacntattg tnttggtttt    120
gtgacccata acttcggaaa ggttgtgttt tatccggcaa caaccacngt gtagcggtgt    180
tttttgtttg cagcagcaga taacgcgcag aaaaaggatn tcaggagatc ctttgatttt    240
ttnttcgggt tctgacgntc atgttgtgtg gaattgtgag cggataacaa tttcacacag    300
aattcaaagg agaggagcca atatagaggg ggaaaaaaaa agaaggggaa agcattagtt    360
taaaaagttg agagaacaaa gtatgttttg cttggatggg caaccaaaga agcntgccag    420
gaatggtcgg taaaaggtgt aagagtcatg aaacgtcttc tgtccaaccg ttaccggaaa    480
catgcaagga atttcttaga ctggccagga ttggattgtg ggaaaggtct cttcaagcnt    540
cccctggct tttatggcaa gaaaatagtg cggactatag agagcgtcgt tctcaaagct    600
```

tgtccccaat agcagaaaag cattgtccta aattccttaa aaggcaccgt gaaataaata 660
ttacgaggac acgatggcac aagaaggagc tttcaactct gccaccagaa cagttatact 720
tcatagtaac catgttgccc tgttcaatga caaggcacgc tctccagcag aaagggaaaa 780
ggagc 785

<210> 50
<211> 889
<212> DNA
<213> Rattus norvegicus

<400> 50
nttnnaaagc ganccggccn gggnggtttg gncggcgctt tatacnaagn cgngccaatn 60
ggctttgggn gggntttcat anggnnntgn tttacccaat tcagtttttt attggtnttt 120
natgggcgca gggatagngn gttcnggntt cccacangaa tttgatttnt ggaatcacaa 180
gtnaccagtn gccgnaatca cgagtttgcc gctttntttc ctaccttana ttcataatan 240
gaatgagtan ttttttttta ttgagnaang ttttnacagg tttagtaaac atgaggacag 300
aggttttaag ttgangatta ggaaggagag ttccggggga cagaatgtgt gtattntcag 360
tcagtgcact acccggaaga gttgcagtca ggttgaggaa gggagcggat ttcctggagg 420
ttttaaccaa cagagagaaa aagcatttac tactgattaa gcacacaatc tctggattca 480
gagaagggtg tttaccttta tataaaatgt ctcctaactg cgtgactgtg tgactttgtt 540
gaagtcaact gagcactgac tgtgttgtgt gcaacatggt aagaggacca actttnttct 600
taaattttat ttattattta tgtcacgtgn acacttgttg cttttgtttt tgttctaatt 660
ttatctgcat atatgtctgc ataccacgtg catttctgat gcntacagat gccagaaaag 720
gacaccgagt ttcccctggg antggagtta tagatggtta taagtctctg agtaggtact 780
gggaagtgaa cttcagtttc ctctggaagg gcagaaagcg cttttcaaat gctgggccat 840
gtatttcagc ccctacttaa tttataattt tattttagag gatgtgctc 889

<210> 51
<211> 947
<212> DNA
<213> Rattus norvegicus

<400> 51
anaaaaatng agaagangag accccagaga agaagnanga gaganaacag agaagaagag 60
agnaagggng anaaantaga gaaaggaaaa gntcttaaag aggcnanaaa ntancnatnn 120
aaggagaaga nggaaggnta acataggagn caagaatana aaganaaaaa gaggtagaga 180
anncagagaa cgagaaaaga tgaaanaaag antanaangg aagaaagang nccagnanaa 240
anaaggcaga aanaagatgn cgtaaaanaa gagagaagat aggnaaaata gaggagaagg 300
ccnaacagga ngggaagagc agcgaattnn agataaaacc ggagganagn nagagaaggn 360
agagntngnn aaggcaaaga cagnanngag nacggtacnt gccccagaag gnngaagaan 420
gncnagangg tgagggnngg cacngnccnt tcccettagg aggncgcccg cccagagatc 480
aggtttcnag gncaccgagt tggatacnag attatncacc naggcaggaa angantatng 540
caaaangatt cggggngggg tcacggggtg agaaataaan tcannaaana gaggacgngg 600
aggagggngg gaaactctng acagaaatng caagcangaa gccagccnca cccaagcccc 660
nacngaagca gcngagangt tgcanggcgg naggtccaaa tcancgnagt catggagnga 720
gcttcgggng ggcccnganc cantgaggaa gggcaggaaa ccatatcnag ccgagccnng 780
nganggntgc cctganacac ccggagaggt aatttttatt tnacgggaag cgtccagnca 840
agttcgtggg ccggaagaga cggtacttta gtatacancg ctnntgctnc gagttgtnng 900
nccttntnat gnnagatctc acaaangaag ctnanaagta gatatgt 947

<210> 52
<211> 860
<212> DNA
<213> Rattus norvegicus

<400> 52
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tttaaaatta aaggggnggg angtttttcc ggttctattn ngccnattcg gggttacact 120
tttatccanc ntttgntttt ttanccggcc gggttaaaaa tgggggggga ttagttcggg 180
taggngttnc cnacagcaca gccctgtttn tcttcgttcc ngaaaaaaaa aaattttgct 240
ggtntcacaa ttttnttaaa caggatttnc ttcaaccatg gattaataca tttccggtgc 300
agnttgcccg gtttgttttt tggntggata gggatgccag caggattcag ggatgcccat 360
tgtgnttagt ntctggccct ttaggagagc tttgggctaa ttatgtgacc gattttaaga 420
agtggtgttg ttgtggttcc agggactcac ggatcagcct ttattttata aggacactgt 480

```
ggaggagaga cagaggctga gctgcattct gatgtcattt gtgctgctgt ggaagttaaa     540
gaaaagctgc agaagtcagc aaaacagatg aataccaaga agggcagtgt gagtacagga     600
atggagagaa aagtcagagt ccagctttgg ttaactccct aggatcagac anttctgcgt     660
aaggacgggt ctacagttta acagaccaca gagcaangtc aaacagcaaa gtggtttcat     720
ggcaggcagg aaatggaaca tttaactgga aacactgaac ccacccatgg caaacttagc     780
aatgaagctg ggtgtggtgg cacatgcctt taattccaac actcagggga cagatntaat     840
gagtttgagg ctagactggt                                                 860
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<210> 53
<211> 191
<212> DNA
<213> Rattus norvegicus

<400> 53

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aggtctgacc acttggaagc ttgccctgan tcatagatga gccactgtct tcttcccctc      60
aattcctcag gatggggaac agccattggg cttttagtag aggagggaca ggcccttttg     120
cagcaacagt tctcccctga atgttggatc tccacctata cacatggggt acttagcctt     180
atggatgccc c                                                          191
```

<210> 54
<211> 988
<212> DNA
<213> Rattus norvegicus

<400> 54

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ttnttggnna cgggtntccg nantatgaan ccnttcccgg ggtttttaaa aancccngga      60
tattcgggga tttgggtttt nnacggcctt tttttnagag gccaaatncc cntntnaang     120
ccttttatcc ttccntttnt gccccncttc naattaggaa gcntggtttg nccgantntt     180
aaggttttta gtcntccttc gttnntnttt cccttntttt ttccctnaag ttataaagcn     240
ggtatntggt ttgccaggnt tctnttgtac ccgtcatngc gggttncggn ttacccaggn     300
tttgttcctn ggccggtncc ttccaatttt ggantntccn ggtcnggngt ccnattncct     360
tgnaacngtt ccacacntna tgacaattaa ttgtttcctg tgtaatttgt ccccggactt     420
ntggattctt gngancaggg cctntgtttc atggaagcaa actcccttaa ntatttacca     480
ggttgattga ttaagaaagt antcatgntt gggaaaccca cntgttttnt tcccaggatg     540
gaancccagg attttggaac tgcagaggct tcagggtctg ggaagcggag gcaggcaaag     600
aatggagtgc actgtccttt tgcaatatgg ggtttgcctg cctgctggct cctctcntgc     660
tntctcagat ggtgactgag gctacttcag caggactagg aataatcatg tccaggtggc     720
tgcccttccg agcagaaagg gacagacgtg ggcgatgaa gttgctatcg ttttttttttt     780
tttctgcaca gactgcaaag tgtgcagagg gagggaggct gtgcaaaaaa aaaaaaaaaa     840
aaaaaaaaaa aaaaaaccga ggacgcagaa gttagactgc tgacccattt ggtgcatgtg     900
tgcccatgga gggaggggac cttctcaaaa gggttcacgc agcangcatt gaaagtnccc     960
cacntgtagg gncgcaagca actgagat                                        988
```

<210> 55
<211> 665
<212> DNA
<213> Rattus norvegicus

<400> 55

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gaaaaagatt caggaanctt atttttntcg gttcgacttc agtnggggaa tgggcggana      60
catttcacac ggatttgtaa anacngtnac ngaaacttgg nggttcgtag atccactttt     120
ttnagacctg agagtagttt ttaaaatatt tnaattaaag gtttcctgca cccacttttt     180
tttttatccc taactttttca tccagtatgg tttttcaata tcacanttta atctaggact     240
ccttgcttaa agcaattaca agttaaatta aaagtaagag atggctnata gctctcatta     300
ctgggatgca ggtgtgaaac aagtgatttg tgtagaagct ggcaggatgg gtataaacaa     360
gaacacgtgc ccagaggatg tattgaaagt tggatttaag tctctgagta gtttatgcta     420
ggcggtagca ttgaacaaga tgaantctct gntcatagag gtagaaactn cccagattct     480
gaggaagtgt gagggagagc attagatgtt actgttgggg atttgggaag gccaggaaac     540
gttactccat gcccaaggag ggtaggagaa aggtttgggc ttagctttga ggacggaggg     600
aactggtggg tggatatgag gatggttatg ctaaaagcag agtggttttc aactattgtt     660
cttct                                                                 665
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<210> 56
<211> 857

<212> DNA
<213> Rattus norvegicus

<400> 56
aaaaaaagaa aggaaagggg aganananaaa annangngan aaaanagana ganagaggna 60
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ggagggaaan agagaanaga gggggagaga anncagagaa nagaanngag aaaaggngga 240
gacnaanana gagggaagaa aagngaggag aagagagggg agaanaaant tgaagaagaa 300
gaagangaga agangagnag aggaaganga ggggaagaag aagaggngga ggagaagaag 360
aggagaggag gaggaaggag aaggaggagg aagagaagga ggaggaagag gagaggagaa 420
ggaggaggat actanggagg ttgtttcaat aaaagagngg gatntaagat taananaagn 480
aataatgccg gtttntatct gttcgggggg ggtccttgtt ctccaaacac agannntgggc 540
cagtttntca aaattnaant gngaagattt cttggntnga gagcagntca gattnantng 600
nattnttttc tagttttnaa cacaanctt gtgntaacaa agagnganga ttcnaggana 660
actcgntttt ntttgggagg agactttgtt cctttcnatg aagatgcagg acgnggaaga 720
cgcagggtgt gaacaggaca cagnnacgct tnngtntntg tcngcntcag cngcgtggga 780
atgagtcaga gcagcacggg gaggtgcctg gatntaagct ttctggtagg gagaacagag 840
tgcaggcngc ggcccag 857

<210> 57
<211> 902
<212> DNA
<213> Rattus norvegicus

<400> 57
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ccgaacttcc ngcaaggaaa aaaaatttgg ngggngtaaa gggcaccncn tcccacaaaa 180
ttttgntaan tttgggcgca aattcangca ggntttngtt ggaaaggngn ananaccaaa 240
gggatttngg ggatttnaaa atcngngttt nnggcaggnn atccngaagt tngaatcgga 300
cgncnaccct ttatttnagc agttatttan gggaacatgg gagggnacca tttcaaacca 360
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ttttccctgn gccagagacc catccangtt ccagcaaaag gntggtcatc tngggcnagc 480
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ggnggactca ggcttgcttt tttttcagga gaggttagat tactaatcat tcagatgttc 720
ataagtcaga acactgagca aagcaatagn ttctcctcca cntactgant cacacgtgca 780
caacagccac acccgcaatg cttntaggag caggtccagn gnacttttgt tttaactatt 840
tntggctctt tattaatcag cacataaata cgcttcgttt ctcctttttc aatatgnatg 900
tg 902

<210> 58
<211> 852
<212> DNA
<213> Rattus norvegicus

<400> 58
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aaatgttccc agaccaaaag gggggggna gtnnaattca nggatcctna ngaggnggaa 120
atttttnnnn tattnaggat caggataaat angaaaangg gnanattttn nnnangnggg 180
tttttttttt tttttttttt tttttnngng gnnnnannan annnnnaaat ggcgncgggc 240
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atgaattcag ntaccaacca ggttggtacc agcattttaa cattcgagtt agacatcaat 360
ggttaggtcg ggagtgagag gttcggggcc ngacatatat tcntggtgaa cccagtgcac 420
cttntggttt ntacaaggag cttgaggtag tcgcccacca gtagctgtca ggcaggtggc 480
ttaagttcag aaccgnttcg tggaacccga gaagcagaaa aagacataag ttntgcngct 540
tcanaatcca ctcntgaata cananatctc ggccaaagaa gcacagccag tctttccgtt 600
nacangaggc cgggagcaac aantccacag ccagcccaag ganatacaaa ggacttgggt 660
cagttctgna ccagttggag tcagagatgg ggccctcaaa gtcccagcag tgaagggcat 720
ggtctccagc nnacagtgga acctttaaga ggtggggact tgtaggagga gttagataat 780
tggggtgtgc ctttgtcccc nacntcgttc tttccctctt tatggccttg atgtggacaa 840
gattgtttct gc 852

<210> 59
<211> 884
<212> DNA
<213> Rattus norvegicus

<400> 59

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ttaaaanaca aaaatttgan ggggnnggng ngttacaaaa agacaggatg ttttccgagt     180
cggattcaat cccaccacaa catggggttc acaccatngt aaggaatcgn tgcctttttg     240
ggggtatcct agggggtana nttccaaata nngataanaa tttttttaaa aatttaattg     300
tanatattta ttanataatt taataaataa tatttggana nantnatgtt ctngcgcctt     360
gnggactggt agttttttnt ccnnattnna actttcccag nactnggtag cctatgtgnt     420
tatgcaaccc nttagaagct gccttcanta ttnaactcat actgtttctc gataatcngg     480
ggagtagctc cagttngcta tgaagctgcg gaaaggtagg cggacatccc aggcttagac     540
agagttcagg ttatttggaa ctttnnaaca gaagtgtgtt cntgcacggc agcaagacna     600
tntgggtccc gtagttccgg tcgccaggag tagtgtattg cttaggacca ttctgggtgg     660
aatgcatctg gtgggtctta aannatgtca ggcagggcct ggcaccaggg tctggcggga     720
agcctcacat accgttntaa tgacttcatc tgcttagaat ttgtggggaa acgatgcaga     780
aaaatctaac cagggatgtt tctgggccag tcatgttggg gatgcctcag tcatgtaaaa     840
ttgagctccc cctggagcac accttaaaac atcttctgtt taat                       884
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<210> 60
<211> 955
<212> DNA
<213> Rattus norvegicus

<400> 60

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tagggnttcc nnntttcccc gganccgcca aatgngacac caaaanngac cgnantcttt     120
ggnngttgct tctcttggan cgcnttttgt tcgaccgggg tgactaaggn catgtngggg     180
acgantaatt gtttccgggg gcngntcggc accttccnan gngngngngg tttggttctg     240
gaagnccgaa nnggcatgtn ttaagatttg ccnatccatt tagggttcgt tcaacgcctt     300
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agtagggaga gagggaaggg agatagaccc ggagacagag aagggaggga ggaagggagg     420
gattatcctg taggatgtga gcccagacnt gtctgtggtn tctttccatg acacaagaga     480
ctttntgctt gtccctagaa tgcttcattt tntagtgtct caaacttaaa gggctagtgt     540
aaagttagac tgtgaacann tngtaaacac aggtgacagg aatgtntgtc agctgggccc     600
nttatatgcc acggcagagt ggtacgtgat gcccccacat gttatgtgga agttntcatg     660
cagggcttca gaacacagta gatggagatt gtgaaaatct gttgttnact taagagactg     720
gccccaagga tccatgtgat gntacttctg ttgcttgtgc tttaaaatct tatgtgatgt     780
tttgcagact ccnttcggga ccccagcaca cagctgagag tctgccctgc tggcactgct     840
gcctgtctgc tgaaggggaa cccaggcatt tgatgttggc cggcccaagg aggggctgaa     900
gctantgagc aaggacagtg atagacccac acagnagttt gcaagtaaat gagnc           955
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<210> 61
<211> 1107
<212> DNA
<213> Rattus norvegicus

<400> 61

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ttaaannttc ccccnggntt caaggaaatg gggcttttga ttggcaagga aggaatgggg     120
nttcccntga ancctcctga ggggccaaan attggggggg gttnacaccc ccggggaaac     180
ccttcttgac cccnagaaan gcngtttagn ttcccnccca tgggntccct taccctgggn     240
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atccagtgca ttccaccatt gagccngcag aggttgatng gcaggaangg tttaaccctt     360
ngaccaggag tgacaaattt ngngggacnc cccagtgnga gctcacaaca ngtngacatt     420
gaggcnccaa aggattgttg aggggatgga ttgtgtcgca gtctggttgc ctttatagtg     480
ccagcatcgt tgagccccgc ccagggagtg ttggcacgcc caaaccccna cccagcgctt     540
gaggcaaggc aaacacactt cccagcccct taanttncna cgcctttgtt gcttggacgt     600
cccggantgg gagcaggatg aaggatttta gtgcaggaga agaccagtgc aagccggaga     660
catngagttc cctntaattc ggtgttcagt ttgccnttnt ggcacgtgac tcgtaactct     720
ggtatgtgtg ctgaaccntc taccagccag agatcagtgt ccttaaagtt cgaatcagtg     780
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tgagggggac tgggaacaat actgatgctg ttgccctcta gtggcaaggt caactccaag 840
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tactgcggat taatacattc ttcatgttgt ggtgacgctc caaccataaa gtgattttcg 960
ttgctgcttc ataactatat ttttgctact gttatgaatc gtgacataaa tactgtgttt 1020
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ctgtaggtgg gccaagctaa atgagat 1107

<210> 62
<211> 92
<212> DNA
<213> Rattus norvegicus

<400> 62
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ttacctgtag gtttggncng cttgaaagag at 92

<210> 63
<211> 209
<212> DNA
<213> Rattus norvegicus

<400> 63
aattccagcc catcctgaga cacacagtga ccctgtctca caaaaccagg gaaaagccag 60
gtgcggagtc tcacgccttt aatctcagtc tccggaaaca gaggcagngg gatctctgtg 120
agttcccagg cgaganttct ttgtacaggg nnccctctga annencctga aagatttcac 180
ctgtaggttg ggccnagctt aaaagagat 209

<210> 64
<211> 97
<212> DNA
<213> Rattus norvegicus

<400> 64
acagagaaac agtgtttccg ttccttaaaa cgttgctcta tcttgaataa caagcttatt 60
acatgcgaat cgtattggga acctactgaa ttccgat 97

<210> 65
<211> 1047
<212> DNA
<213> Rattus norvegicus

<400> 65
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atccanaatt naattccgga aatttacaat aatttgaatt ntagttttcc caattntaat 180
ntcagtagtt tgnntttgtg tgccccnatt ntaanatcag acccgtccaa tcacccaatt 240
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ctgtggataa tctctgggtc agtcgaaccg ttttaccatc catttcgtta ctccgagaga 540
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cttgcagcgc gcgcaagacc ctttccagtc tagagcctcg cctagttctg cgcgtgcgcg 780
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aataaatcgc ccccccgccc ccgcttgtgt aaggcgcgct gtatctctgg cattgtgtgg 960
accgcctcac attcataagc ttcgtcagca gcagtagaga atggcttgaa agacnttnac 1020
ctgtaggttt ggcnagcttt aaaagat 1047

<210> 66
<211> 1063
<212> DNA

<213> Rattus norvegicus

<400> 66

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ccngaacagt ccantnttaa aattgggcct nttgggatta acggattcca aggttgcaac    180
anattggcaa gtttnnggac aggaggtttc aantggntaa agtggataaa tngtgaattt    240
tggagangga attgacttgg ttgggggcca aaantaggta gcattttgcc cggagggttg    300
attgcattct gttttgtgta aanatgaagn tacttgacag ctttgagata agaaggagac    360
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ctaatggtgg ctgggttccc agcgagaacc agtgganccc aaggatagct tttggtgact   1020
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<210> 67
<211> 815
<212> DNA
<213> Rattus norvegicus

<400> 67

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<210> 68
<211> 1034
<212> DNA
<213> Rattus norvegicus

<400> 68

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ccttnncngg anaatatntt ttgggccaaa ccngttagnc gggatttccc aattgcgncn    240
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gagaaggggc agaggaatat gagggaagga ttgtgggagg gagtgaccag tagggaaaca    840
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gtctacaaag tcaattactc ctttcccttc ctccaccctt tcttctaata ttaggcaaaa 960
acaaacncaa aaacanaaac aancaaactg aaagactnta acctgtaggt tggncagctt 1020
gaaagagatn tttc 1034

<210> 69
<211> 186
<212> DNA
<213> Rattus norvegicus

<400> 69
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aagaagtagc caccgttgtt ttacttaact catggtccac ggggtgagct gaggtctcct 120
tcctgagcaa gatggaaatt ttacttggtc tgttaactag cgtgcattga atggangaca 180
tatgat 186

<210> 70
<211> 1028
<212> DNA
<213> Rattus norvegicus

<400> 70
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cttaaattta ggnatttttg aatnatttca acccnttgca ggcagtttgt nccatgttnt 120
gggaaagttt taacaggatg gttatttnga caaaacaggt tttttcagac catttgtgna 180
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aaaagatc 1028

<210> 71
<211> 1034
<212> DNA
<213> Rattus norvegicus

<400> 71
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gaaagagatn tttc 1034

<210> 72
<211> 824
<212> DNA
<213> Rattus norvegicus

<400> 72
gggggntttt cnnanntanc aaaaantngn tntancanng antnnttgag ntgttgaagn 60
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atgntgtcag gagaaacccn ttcagtnttg tgcaattggt tcgccagcag ttaggaccgn 180
ttccccatca cttgtgccag cggacatcca gntattgagc cntgnatcat ttatggnaca 240
aattaggaac acacaacaga gatccgcttt ntgactgcca tgttcgccaa actcaattgg 300
gggaagtaat cctccagacc gttccgtttg cacgtntagg aagccacagt gaaaacacaa 360
aattcgtgga ggcgactcta accaggaagc ctaatcccnt agattcccgg gacactgggg 420
caggcgtcct aaaaacagct ttgtggggct tcagtcctcc gtgcggttcc agtccgggtc 480
ttggggatcg ccctcgcggg gaatgtccgg gactccggtc ggtatctttt tggcctggga 540
atttccagcg tgtggaaaaa gtccacaaac ttagtcctca ctgcccgcct cgcctcctcc 600
ggcccttctc ggtgcccacg caccccccga tcgaacccga ggatgagcat agggtgtatt 660
ttaggcgtgc tgggcttccc cgccccccctc tgcccactta gctggcaaga agaaagccag 720
cactataaag gaggccaggg ccaaggactg gcctcctctt gctcacgagg tcagacgcga 780
gctctgaaag acttcacctg taggtttggc aagctgaaga gatc 824

<210> 73
<211> 774
<212> DNA
<213> Rattus norvegicus

<400> 73
gaggggganna ncancaggac caancngata agggggtcaa caacntgngt tccncccntt 60
gagngggaaa tgagcacgng gcantccaac cgntcaaggt cccgnttcgg acggtcacac 120
antaggttnt catntggatt gccngngttc cngttggcat ccgggaaaan tgagactgtg 180
tcggtaccag agntaggatg gccntccttc ccngccccgg ccttnttggc gccttgcgat 240
ccttcccgaa ccggcccntg gcgtctccgc cttnggcact tgcacatntg gcggcccagg 300
atggcgcttc cgggatggcg ccagcgcgcg tacgtcatca cggagcgtcc atgtgttcct 360
tctgtccaag cgcntaggag cctgcgcgta ctcccagcaa ggaagatgta ggaccaaaat 420
gtagaagcac ttaacatgaa cgtcaaaacg atgaccaatc acagggcgat atatgcgcat 480
gcgcaatgtt ccaatcatgg ctcataagca atccggaagt ggccaattaa atatactatt 540
tactaatcca gggttacaca gtgaaaccct gtctcgaaaa ataaacacag ggctggagag 600
atggctcact gattaagaac actgactgct cttccagaag tcttgagttc aattccgagc 660
aagcacatgg tggctcacaa ccatctgtaa cagattctgg tttatgtnga gacaactaca 720
gtgtactcgt attgaaagnt ncccacctgt aggttnggca agctaaanga gatc 774

<210> 74
<211> 248
<212> DNA
<213> Rattus norvegicus

<400> 74
tgacacttca tggaaactga gaccgggagc ttccaccaga aggcactgcc cagtggagaa 60
aaccgacttc tttttgttgt tgttctgatg ttttgttttt gagataaagg tctcactgtg 120
tagctcaggc tggttttgaa atcaggatcc tgaccctcag gaatgttaaa gtgcctaaaa 180
gtggngacaa attattttac gtgcctttga aagacttcac ctgtaggttn ggcnagctag 240
aagagatc 248

<210> 75
<211> 833
<212> DNA
<213> Rattus norvegicus

<400> 75
aanggggtta tnntggagan atnctaagnt cccaaagcaa nttaggattg ctnccnnnng 60
aattnttaag cntttgcatt aagtantaat gccaaaatga ccccaanata tngntccttg 120
antgtnntaa aaangaggat cttcnttgnc catanacgcc ntatatgaaa gcaactgaac 180
aagatttaaa attggacagg tcacaancgg gcgtgtgcct ttaatcccag cactcgntgg 240
ctgatagaag cagatgcatn tatgtgggtt tgaggacagn tngnttnacg tagagagttc 300

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ntatatcagt agggctttgt agagaccnta tctcaaaaaa caaaagcaaa acaacagaga     360
aaaaatcaat tgaccatgtc ccaattacct ttatttatct gtaacctatc cttagttata     420
ctcgtaatct ttttctctct tcagtttgcg tacgggacag cagacctact cacaacccaa     480
gctntaaatg atgagcgtac tcagccaggg agcttcaccc cacttaaccc cataagatgg     540
cggcagcgcc tcttcaccca ctcagggctg aagcacgcat cacgtgatgc gctccagctc     600
tcgccgcggt ggctgacggg aggtggagat agaacgaggg tgtcggccat tttgtgtctg     660
tttcctgccg gacgtggtgg tggcggttgg ttccgagaac tgtgcgagtc tcttctctct     720
tttttttttt ttgtttttcg ttttcccccc agcttctttt cgcctctntt ctgcatagtc     780
tgtagtgcgc agttgaaaga ttccacctgt aggttgggca agctaaaaga gat            833
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<210> 76
<211> 880
<212> DNA
<213> Rattus norvegicus

<400> 76

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aanatggntt ggttntaaag gttaaaattg gggcaaaatt tttccgcccg ggtccttaaa      60
ccggattaac tccaaggcca aaattccgag ggggaatcaa caacaaggac ccaaccggat     120
taaggcgggt tcaaacaaac ttggatttcc ngccctttgg ggcgggggaa atgggcacgg     180
gngcattcca agcngntcaa ggttccggct tgcggacggt taacacaant aggtttctca     240
tctagattgg ccngcgttgc ggttgagcat ccgggaaaat tgagattgtg tcggtaccag     300
aggtaggatg ggccttcctt cccngccccg gcttcctggc gccttgcnat ccttcccgaa     360
ccggcccttg ggtctccggc cttgggcact tgcacatctg gcggccagga tgcgcttccg     420
ggatggcgcc agcgcgcgta cgtcatcacg gagcgtccat gtgttcnttc tgtccaagcg     480
cttaggagcc tgcgcgtact cccagcaagg aagatgtagg accaaaatgt agaagcactt     540
aacatgaacg tcaaaacgat gaccaatcac agggcgatat atgcgcatgc gcaatgttcc     600
aatcatggct cataagcaat ccggaagtgg ccaattaaat atactattta ctaatccagg     660
gttacacagt gaaaccctgt ctcgaaaaat aaacacaggg ctggagagat ggctcactga     720
ttaagaacac tgactgctct tccagaagtc ttgagttcaa ttccgagcaa gcacatggtg     780
gctcacaacc atctgtaaca gattctggtt tatctggnnt cnactacagt gtanngcat      840
tgaaagatnn tacctgtagg ttggncagct aaaaaggatc                           880
```

<210> 77
<211> 864
<212> DNA
<213> Rattus norvegicus

<400> 77

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aattttaant tgttggnata anggcttgnc catatccttc ctnttgtttg ccctaagtaa      60
cagccaattg ggggagaant tttntgtcag tatcatattt ttcgttaggg aacggaggcn     120
caggaantga tccntntggg ttacagtcat tttagcatag gntgacagtt ggngaccaan     180
tnatcttgcc gtgttggaag gagaggggan taaggntgaa gctcttgagt ccnttgangc     240
ccttggaatc gggaantccc ttaaaccaac ccctttttgcc gttgaattgc accaaccaga     300
ttcttccagt ctgcttgagg angacaggac ttcattgctn tggagagggg caggagggtt     360
gggagttgac ntnacagggc tcagggattc ttttagaagg gtccaggttc atggcttccc     420
cccccccccag ccaggtcaga cactaaagtg tcttaagccc ctccatactt gccgctcccc     480
cacnttggat gaagccggcc attaggcagg gaccgtctct gggagaggcc aagccctctg     540
gctcacttgt ggatttcctt taagcaagac ttcctctctg cttccaggac tcctgtcaaa     600
caagagggtc cctggcttag agtttgggag ctgcaggcag aacagacatt ccccgatgac     660
tcacaagcct ggaactctgt gggccagcag gaatggggat ggctttctgg tcagtcaggg     720
tcaactggga cactcactct gagacaggga ggcaagggag aaacaggtca gaggtagaga     780
gagctcagtc ccagggactc acgttgaggt ccctaaggtg cgctagggag aggnttttac     840
attcggttng gcaagctaaa agag                                            864
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<210> 78
<211> 874
<212> DNA
<213> Rattus norvegicus

<400> 78

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gaggttggac cacaaggagn ttggnggaaa atnnaaaagt caacctatca gggtgtcttt      60
tagtttggaa cagaggcttg ggcagaaata tgggcaagta ttaggaaagt acaaggggaa     120
atgttgtcaa cgcgnttgtt ttcccagttg ttgnactgat cccnccagga tgttttccca     180
cntatgntat ggaaccntct ctttcaggaa gccattntna ncntatggnt tgcaacccct     240
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```
ttggggtcgc aacagcaggt attaacatta ggattcataa cgntagcaaa atnacagtta     300
tggagtagca atgaaataac tctatgnttg ggagggtcac cacaacanga gggacggtat     360
cacaggnttt tagcattagg aaggttgagg accttatttc agagtgtcnt gacaatcntt     420
cntgggacca cttgacttna tctggagccc tttccctcac gctcntactc cttaccatct     480
ctgcacagct ctntgaggct tagagcggtc tttcttcata gctttccntt ttccttcagg     540
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atagtttccc acatatgagt cctcaaccgc cccacatcac gagacggaca agaccggaga     660
cgccatacat tctgtatttg ccctccttcc tcatttaaat aggaatttgt tgctgtttaa     720
tttttcatta tttgtgtgtg tgtgtgtgtg tgtgtgtgtg tgtgtgtgtg tgtgtgtgtg     780
tgcgcgcgca cgttaatatg ccgctcagaa tagtctaaaa ctgctgggct tgaaagacnt     840
ncacctgtag gtttgggcna gctaaaagag tatc                                  874
```

<210> 79
<211> 886
<212> DNA
<213> Rattus norvegicus

<400> 79

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atttttnaat tgcagcaatc ctcctgcctt ttttcttggt tgttaantca caggatnttt      60
gcacacttga ggttgaantt gcagcaatcc tcctgctttt gtttnttggg cgcttggatt     120
atagtatgtg cataacactt gagcagtaac tgttttcttc aatctcattt atctcagaag     180
ttccccttgn tgattcagac gttattaatt aggcaaacca atgttgattg tcattaccca     240
tgagttgctt ggcttgtgag atgcatactg tgtgttcgtg aggcacntac tgtgaggcat     300
gtgcccgtga ggttcatggc tgtgaggtgt gtgcccgtga ggttcatggc tttctngacc     360
acngggagta tgaaggagag gaatcctacg tttgatgcca gccagggtta tacagcaaga     420
tcccgtctca aaacaaaatg aagaagtaga gagattagtg ttaataagca actgaggcct     480
tgaagggctg aggtcaggcg gtgccctggt gcacacacag aagcgtgcca gtgacgtcag     540
acagactcag ccctgtgtca gacaggccgg agggtgactg gccatgtggc gtgattggac     600
acattcccaa aaaaggaact cgatggaaga ggctcctcnt gctccagaca gggcggtggt     660
tatgtgactt gtgcgagatt agtctcatac cctattgcta gcctgtgcct ggtaccacgg     720
acatggtaca atccagggag gagccgtaag cactacaggg gagccatcct gaatcccagc     780
aagtccaact tctgtttttt cttccttccc cgcaacatta ggaatgactt ctaagagngc     840
tgttgaaaga ctttcacctg taggttgggc aagcttaaaa gaggat                     886
```

<210> 80
<211> 865
<212> DNA
<213> Rattus norvegicus

<400> 80

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tggaggtaaa agtcacaagn ttttcaaggg tttgagatga cagttcaacg tgagnattng      60
acaaggattg attcttgtnn acaggaaagn tcccccatccc accaananac accgtgttca    120
ggcccantgc tcagagctcc gggcgccagc gaagggcaaa cggccactga ttggaaagnt     180
gcagtttaaa gacatgtccc aggaactggt anccttgtgt gactggactt agccttgcaa     240
ntctgtctga agcataacnt gntgctgtct ntgggcgagc atttatgtgc cccacttgag     300
acccatctca ggacacgcag gacacggtcc agtggagctt tccctccaga gagaggtgtt     360
agggnccatc agtgagcttc caaggacagg ggaccagaac ggtgaaaaca aaccagggct     420
gtgaaggaga gcagggcggg gggggggga gggggggcgc tctntagaat agattgaacc      480
tgcagagctg cttgctacct gaagttgtca ccctttttacc cacccacntc atctgtctct    540
gcttgaccat ctcagcaagt gtcacctcgc tgccaggaca caagtttcct aaagcttatt     600
tcagtgtcag ccgctgggga gacacattca gggcatgggc gtcccccagc cctcggggag     660
aatgtgggag gtggcgatgt gggagggatt cgagagaaga gaatgcttaa gaaccatcca     720
gggaacctgt gcgtttgaag gtctgagtta cacacaggct gctcaggaag gagctagagc     780
tccaaatagg agctgtgatc aggctgtgtg tgtgtgcctg gtgaaagact ttnacctgta     840
ggtttgggcn agcttgaaaa gtatc                                            865
```

<210> 81
<211> 859
<212> DNA
<213> Rattus norvegicus

<400> 81

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cangagcant ntgaancagg catttntgga agggctccng agaaaacacg tggaattnct      60
tgtctctggg actttagtnc cagcnaggan gatncagtga gggaacacac cgggcttttg     120
```

ttgtgcacgg gaggccaggc tcancnncct tgggagnttg acatccagca ggctatanac 180
agtgatccag gggacatgta cacatgggga actgnccagg cagagaaaga caagagaaaa 240
tctcaaanga tgaagacaga gangagtaat atggccagaa ngatacagtg cctcntgcat 300
aacccttgag tttaatttcc agggtcaact gtattttgaa agtataaatg aaagttcctg 360
aagtaataaa tttataggat gttagtatca cactgttcag aatagctcaa aaaatcctgc 420
cntgtcctct taagtatgtg aatcatcttt tactgcaacg tgtccacaat gtatatacta 480
catacccaaa agtcctcact gttatcccaa ttagtaggct ggctgccaat agttgtccat 540
acagagtgcc tgctgctgtg gccatccnta ctgtagtaaa cagtcatcca aagctcagga 600
gtgaggctat tgtagaaatg cacttcctgg gggccctact gtcagtgagc acctgagaga 660
gaaagggaca caggcccaag gtgggaggcc ttagataaag gcccatcatg ctcaggaaag 720
gatttntaca gatctcttag ggaagttaca atcaaattca tacctcacag cagagctcag 780
gagaagaatc cataaagnnt gaagacatgc ttgtngtgnc tgaaggacnn tacntgtagn 840
tngggccngc tgaaatttt 859

<210> 82
<211> 1021
<212> DNA
<213> Rattus norvegicus

<400> 82
caatngncaa aggtttggaa cccgngaaat ttnaaaagtt tgcgngantg gttgacnttc 60
cnggtgtnaa nggtttcccc gttcngattg nagggatcnc ttttatccct tttttnagnt 120
ttttttgag nggaattttg ggttcnaant gngttaccct taagtaaccc cattttgcan 180
ggcatggaaa atacctaaan tgggatngaa agttcanatn gaggtcagga anggntggaa 240
cagggtngac cggttngacc gttggacctt tgaganccat cagatntttc ccaggttncc 300
ccaaggactt gaaatgaccn tgtnccttat ttnaantacc caatcagttg gtttctcgct 360
tctgttcgcg cgtttttgtt cccggagttc aataaaggag cccacaaccc ntcantnggg 420
cgccagtcct ccgattgact gagtcgcccg ggtacccgtg tatccaataa accntcttgc 480
agttgcatcc gacttgtggt cttcgctgtt ccttgggagg gtctcctctg agtgattgac 540
tacccgtcag cgggggtctt tcaaactgca gttctcaagt aagctcaacc atccgagggt 600
cattctcaaa gccaagtcaa acttgggagc cctcactcct ggtggtcttt caaaagaccg 660
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tatctgatgg gattntaagt ccctgggcag acccgggttt gtgggcctga agcttgagtt 960
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g 1021

<210> 83
<211> 1013
<212> DNA
<213> Rattus norvegicus

<400> 83
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tcacatgtnc tcacacanat cngggggacn ctcacancnn catctcacnt ntgnganctc 120
acactcgtgt gggntctttc aaaacantgt ncnntggata cncagacact cnncnagngn 180
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nnggcacata tntntgacac ngnggtatat nngnctctcn ggnganacat ttgntncgca 300
caaaaanccn tggagatttn tctacncaat annctanttt tcacaggnga gcncntgtnn 360
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cccgnttntg tgnnccaaan tnttgttttc caagacatat agtggnacat gnnactctnc 480
gatntccgat gagnananat gtgntcngac ntttacagcg natacacngt ggngcanntn 540
tcacagatat gtgtntatnt cnnacanaca aatntgcnng actcctctcg tgtataaatc 600
aatanacggg ngggttaaca tnnggccncn gttgnncagt natancgnga aacacactcn 660
caagggctnc aanttttnca nctatacacn cncncccgan gggncngngc acaaatgtgc 720
nccgaaattt tatncgccnc naacactctn aaattnntcc cgggacccta gatatatttn 780
tccncattna aaatttgcac attntttncc anttgcangg gnantcgggg gttcacccnc 840
cncnttggga aggggnntnt tnaacccggg ttcnaantta tagggggggtt tanatcnccc 900
catttttna aaaagngttt accntgggcc ccntnttttn cnaaaaaatt tgnccccgnt 960
ttancnccgg ggttggggaa cncgaatttc ttngggngcc cccctnagnn ttt 1013

<210> 84

<211> 1002
<212> DNA
<213> Rattus norvegicus

<400> 84
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gttccccngt aatggatact aggttgaact tccangggga antattattt caataaggtt 120
ttagaggtcc cacttgtnat caggttattc tgttgctttg ggtcaagcaa acagccnatc 180
aggattgtga ttattngant aacccattta cctnacagcn gggaggaaan ccaangggag 240
gcttgaggaa acggcttgtg ggttcataaa ctctttgaat catacсttgg gtgattcaaa 300
tgctttttac taggctctcc tttcatagta cctctcttgt ggacaaggac ccagtccttt 360
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ttttcaacaa ttacaaagac atttctgggt tggactatgc attcctttgg gccagattct 540
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gaaatccata aagctttaaa tgccttctaa atagccaata ttttaatgag aaatgtagtc 660
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ttggttggtt ggttggttag ttggttggtt ttggctttgg ttttctgtcc catggtaata 780
tgatacttat gtcatagatt agttaactca aatggtcttt tcaggtggca gtctggaaaa 840
caactaactt gggggggaaaa aggctgctcc atgttctata aaagctgtac atgtgatttt 900
ctctgcttta ccttttatac tcatttattn tgttatttgt gtatgaaagc cttccgtatg 960
aaagaccntt acctgtaggt ttggggngct agaaaagatc tc 1002

<210> 85
<211> 1031
<212> DNA
<213> Rattus norvegicus

<400> 85
caacnnccat nttttggaat ttgnggggta aaatttaaac cgattcnttt tccncaaacc 60
caantggggg atatnnatgt atgtngtagg gtcccccngt aatggaatat ttaggttgaa 120
cttacaaggg aaatattatt ttcacaatgg tttagaggtt ccactgtnac aagtattctg 180
ttgctttggn ccangtcaaa cagcccatca ggatggtgat attagaatta accatttatc 240
caacagccag gagaaancca aagggagctt gagaaacggc tgtgggttca taaaactctt 300
tgaatcatac cttggtgatt caaatgcttt ttattaggct ctccttcata gtacctctct 360
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tcagctttaa tataaattag ctttctaagt tcagctgacc accttttcac tggaccttca 480
ctgatctcac agggaagata tattttcaac aattacaaag acatttctgg gttggactat 540
gcattccttt gggccagatt ctacatcctt tttttatgcc agaatttttt agcgttcctg 600
taagattgtc agtttcccct aggaaatcca taaagcttta aatgccttct aaatagccaa 660
tattttaatg agaaatgtag tcactgatat ctctttgtat ttaaaggtta ttttgagggg 720
agttgcttgg ttggttggtt ggttggttgg ttggttggtt agttggttgg ttttggcttt 780
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taaaagctgt acatgtgatt ttctctgctt taccttttat actcatttat tttgttattt 960
gtgtatgaaa gcccttcncc tatgaaagac nttcactgta ggtttgggcn gctagaaagn 1020
gatcnnnaaa a 1031

<210> 86
<211> 1039
<212> DNA
<213> Rattus norvegicus

<400> 86
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nanaccccaa taccttggat nttttaanat gcncctgggt aagcnaantt gaattatttt 120
ccntgggata anaagtggaa tcattgacag ttttgtggtc cttttnncat ccccatgngg 180
tttnatgact aggcacttta tttcatggac aaaccagtgt tgtccctcnt ggggactgag 240
tgggattaaa aaaaccttcc aaaaatgtgt aatntgatca aacccattga gacaatcagt 300
gnggagtatt agcaaattaa actgacttgt tcacttntga aaantgatgt ctgatttcgg 360
aagaatccca gtgcctcggg acatgaaagg gagatgtaac cttgagttca tggttaggag 420
ggaattcata gagacagttg gtaaaaatct gagtgaggtt gagaggttgg aggaccacat 480
tgtgtatttg ctcatcntgt gagggagaga ctttgtactc tgctctgaga aggcagaact 540
gttaggcaga cacttagaga atatatgtca tggcaaaaga catccaccca acaagtcttc 600

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agtaacaaag cactaaacag aaaggggttg aagagactgg tcagtggctg agagctttta     660
ttgctcttac agaggactcg gcatgcntag cagctcacaa cagcntgtga cttcaacact     720
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aaagaaatct tttaaacatt gagcaaatgt aatcaggtac taacattgaa tatatctggg     840
gccaggaatt attctggttt attgcctttt tcggaagcct aatatcacac atagagaaat     900
aggcagcaca ggcctaacag cccataatgt gtgctattct atcaatagtg ccaagtattg     960
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<211> 1058
<212> DNA
<213> Rattus norvegicus

<400> 87
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<210> 88
<211> 1043
<212> DNA
<213> Rattus norvegicus

<400> 88
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<210> 89
<211> 454
<212> DNA
<213> Rattus norvegicus
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<400> 89
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<210> 90
<211> 873
<212> DNA
<213> Rattus norvegicus

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<210> 91
<211> 876
<212> DNA
<213> Rattus norvegicus

<400> 91
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<210> 92
<211> 459
<212> DNA
<213> Rattus norvegicus

<400> 92
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<210> 93
<211> 3133
<212> DNA
<213> Rattus norvegicus

<400> 93
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<210> 94
<211> 2161
<212> DNA
<213> Rattus norvegicus

<400> 94
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<210> 95
<211> 824
<212> DNA
<213> Rattus norvegicus

<400> 95
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<210> 96
<211> 774
<212> DNA
<213> Rattus norvegicus

<400> 96
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<210> 97
<211> 248
<212> DNA
<213> Rattus norvegicus

<400> 97
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<210> 98
<211> 880
<212> DNA
<213> Rattus norvegicus

<400> 98
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ttaagaacac tgactgctct tccagaagtc ttgagttcaa ttccgagcaa gcacatggtg 780
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tgaaagatnn tacctgtagg ttggncagct aaaaaggatc 880

<210> 99
<211> 864
<212> DNA
<213> Rattus norvegicus

<400> 99
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caggaantga tccntntggg ttacagtcat tttagcatag gntgacagtt ggngaccaan 180
tnatcttgcc gtgttggaag gagaggggan taaggntgaa gctcttgagt ccnttgangc 240

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ccttggaatc gggaantccc ttaaaccaac cccttttgcc gttgaattgc accaaccaga     300
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tcaactggga cactcactct gagacaggga ggcaagggag aaacaggtca gaggtagaga     780
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<210> 100
<211> 874
<212> DNA
<213> Rattus norvegicus

<400> 100

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tgcgcgcgca cgttaatatg ccgctcagaa tagtctaaaa ctgctgggct tgaaagacnt     840
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<210> 101
<211> 886
<212> DNA
<213> Rattus norvegicus

<400> 101

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atagtatgtg cataacactt gagcagtaac tgttttcttc aatctcattt atctcagaag     180
ttccccttgn tgattcagac gttattaatt aggcaaacca atgttgattg tcattaccca     240
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acattcccaa aaaaggaact cgatggaaga ggctcctcnt gctccagaca gggcggtggt     660
tatgtgactt gtgcgagatt agtctcatac cctattgcta gcctgtgcct ggtaccacgg     720
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<210> 102
<211> 865
<212> DNA
<213> Rattus norvegicus

<400> 102

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acaaggattg attcttgtnn acaggaaagn tccccatccc accaananac accgtgttca     120
```

```
ggcccantgc tcagagctcc gggcgccagc gaagggcaaa cggccactga ttggaaagnt    180
gcagtttaaa gacatgtccc aggaactggt anccttgtgt gactggactt agccttgcaa    240
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acccatctca ggacacgcag gacacggtcc agtggagctt tccctccaga gagaggtgtt    360
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ggtttgggcn agcttgaaaa gtatc                                          865
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<210> 103
<211> 859
<212> DNA
<213> Rattus norvegicus

<400> 103

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ttgtgcacgg gaggccaggc tcancnncct tgggagnttg acatccagca ggctatanac    180
agtgatccag gggacatgta cacatgggga actgnccagg cagagaaaga caagagaaaa    240
tctcaaanga tgaagacaga gangagtaat atggccagaa ngatacagtg cctcntgcat    300
aaccccttgag tttaatttcc agggtcaact gtattttgaa agtataaatg aaagttcctg   360
aagtaataaa tttataggat gttagtatca cactgttcag aatagctcaa aaaatcctgc    420
cntgtcctct taagtatgtg aatcatcttt tactgcaacg tgtccacaat gtatatacta    480
catacccaaa agtcctcact gttatcccaa ttagtaggct ggctgccaat agttgtccat    540
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gtgaggctat tgtagaaatg cacttcctgg gggccctact gtcagtgagc acctgagaga    660
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tngggccngc tgaaatttt                                                 859
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<210> 104
<211> 883
<212> DNA
<213> Rattus norvegicus

<400> 104

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natctcnccc cggtttnaaa acccncaatg gggaaaaagg tacancngat tntttatngg    120
tttgggcgga gggggaaatt tttttggttt ttttntttnn gggatttttg aaaaaaaaan    180
gaanttttta ggtttcccnn angtaattta tttcaatgga ccatttttgg ggttctccct    240
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ttataagagc agagaggagc tttaccaggg acaggaaggc aaaagagctg aatnttaaac    480
aaaagaataa gaacaggatn tcatctgtga gctgtcacag tgggtttgca gagcaggaga    540
acacagacag gattagctat aaagttgtta cattagttat tntattggag catacaatac    600
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nacaccaaat tgctttagaa aatgctagnt ctactgtccc tgtctattgt cagctttgca    780
atgtgcatag tgacaggagt tgcctgggag cttggggctt atgttttgca gatccattgt    840
aattaaaaaa gaattgtaag gagatggagg cacggggtga ggg                      883
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<210> 105
<211> 987
<212> DNA
<213> Rattus norvegicus

<400> 105

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ggngccaaan aaggttnatt ggaggncnta tttgaattgg tntgtaaanc ntttncttgg 180
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<210> 106
<211> 1031
<212> DNA
<213> Rattus norvegicus

<400> 106
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<210> 107
<211> 1138
<212> DNA
<213> Rattus norvegicus

<400> 107
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nangannnaa nccggngnna ncanncagnn gggaaacagc ccagagagat aggacancaa 180
acnaganagn acacancgng acgagananc ccgaaagnnn nanacnnana nanaannaag 240
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gnngcgngan cnanacacga cngaagagac gngngcngaa naganacncn gaanngnaac 360
aagangnana annngacagg aancacnnag nagggngngg gcaagcgcaa ngnnnganaa 420
nnnacaacag aaaaagannc anancanaag ngncgagagn annagaanna gngaaanncg 480
nanncgcncc gaagaagaac gnnggacaaa naccgacgna ncnnnnncan ngannaaanc 540
gcangnancn gacnaggaac gacngnaagn gcnaagnnac ganngncaga nnanangaaa 600
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<210> 108
<211> 1072
<212> DNA
<213> Rattus norvegicus

<400> 108
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<210> 109
<211> 1094
<212> DNA
<213> Rattus norvegicus

<400> 109
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gctaaaatga gatc 1094

<210> 110
<211> 1107
<212> DNA
<213> Rattus norvegicus

<400> 110
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<210> 111
<211> 1069
<212> DNA
<213> Rattus norvegicus

<400> 111

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ctctcactgg ggcgtccctc taagatctgt ccactcctgg tntaggggtt aagcctttcg    1020
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<210> 112
<211> 1058
<212> DNA
<213> Rattus norvegicus

<400> 112

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tgggaaccng acgggtttaa gntaccgggt ttccccntgg agtccntggg ggttcctntc     120
cgaccttcgg ttaccggtac ctgcccnctt tttcctttgg gagggtgggn tttttcatag     180
ctcagctgta gtatctcagt tcgtttagtc nttngnccaa gttggtttnt gcaggacccc     240
cngtnagccg gaccggtgcc ccttatccgg taatattgtc ttgagtccaa ccngtagaca     300
ngattattgc cattggcagc agcaatgtaa caggttngca gagcgaggta tgtaggcggt     360
gtacngggtt cttgaagtgg tgccntaant tacggntaca ntngagggac agtatttggt     420
atttgcgctn ttgttgaagc cagttacttt nggaaaggag ttgntagttc ttnatccggc     480
aaacaancca cngttgntag cggtggtttt tttgtttgca agcagcagat tacgcgcaga     540
aaaaaagnat ctcaggaaga tcctttnatc ttttctttcg gggtctgacg ctcatgttgt     600
gtggaattgt gagcggataa caatttcaca cagaatttct cttagaaaaa tctgtccttc     660
agaaacttaa attctgctgt tccataacag aagtcagcaa gtgactcacc ctccagatac     720
aggtatatta cctccactcc catccacaga gacttaattc tagtcagctt catgatagtg     780
agccttcatc cgtaaggagc tgtatggtat gggaagggga tacagacagg gccaggggtg     840
tttttaaacg gtaacccagg gaccacatcc attaaaaaca ctggactgtt tgtgagagtg     900
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tatattcctg agcattgcct atcccttaag gtactacaaa atttgggagt gaggctcagc 960
aaactatttt aacatgcctc tcccacccaa ctactcaaga ttccccgtgc acagttgaaa 1020
gntttnccac ctgnaggtgg ggccaagcta aaagagat 1058

<210> 113
<211> 1046
<212> DNA
<213> Rattus norvegicus

<400> 113
cannaaaann agttccaagg aantggntgc ccngaacaag gacccaaaac ntgnnnnana 60
anggggggann naanggcana annnatggac gagagtnaan ancgcnangn agaagantna 120
aaantcncca nntggngccc caaatnncnc aattgancca aancnntaga ggnncccaag 180
acnaatgggc actntganna gancnggcca gaagncaagn gggggannnt catagnnaca 240
tggnanaaat aaagntntgt aaacccggan tggcaatnga aaccagcaaa gacccatgaa 300
cgtgagngan accagttgga aacaatgaan nnantgggtn antnacagga atgnggtnan 360
gacgcnnagt ganccccaaan aggcaacncc attgaaagcc ttcnccncca tggaaatact 420
gtanntaaaa caaacaaaca aatnacaaaa anaaaaaacc caaagcttaa gtggagtgcc 480
cnttccagnt agccaccnnn taagaactgt aaatcgcacc ntcccangcc agatgcaggt 540
aaggnaggat tacaggnatn tcggagggct caggagggaa tgggtcncaa nntgagctga 600
ggcncnggtg anttncgcta cntcgnaaaa aangagaagt catgtgggac gnatgtgtgt 660
aagcacagct cntgtgangt caagtcagca acantatgcc atactctgaa gacagaggnc 720
cataatagna ttgttacang atncnngact tttanaaaan caaaatccta aatcctattc 780
tccgtgggcc cacacgaaac anccatccat caggatcatc tcacagttgc ctctgannnt 840
tngtnttctn ggaancntan gntntcggag ttggggaccg aactcagggc cgtgtgcttg 900
ctaggcaagc gctctaccag tgagctaaat ccncaacccc cacagntgcc tcntntgatt 960
gnaggtntcn tatcccnttc ttttgtggca agntcttctg ggccccntga aagtgaannc 1020
acntaagngg ncgccagcta agnaga 1046

<210> 114
<211> 1083
<212> DNA
<213> Rattus norvegicus

<400> 114
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ttgnntgggg tgaattcccg ccntngnttg gaggaggnaa ttatnttgta gaaatttatg 180
gttgtggggg atnttgttaa atcttttgaa tgtgttcccc ttntgtttcc cttttgggac 240
atggntctta ataggtggnc aaattttacc ntnttggaat cagcctattt atcaagatta 300
gcccagtgtg ctcaaccttg tggaacccct ttaacaggat ttgcttggnc catntgaaac 360
acagtattta tgtcaggatt cataacagta gcaaaantat agttatgang cagcaagaaa 420
atcactttat ggttggagcg tcaccacaac atgaggaatg tattaatccg cagtattaga 480
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attcgaactt taaggacact gatctctggc tggtagaggg ttcagcacac ataccagagt 660
tacgagtcac gtgccagaag ggcaaactga acacggaatt agagggaact cgatgtctcc 720
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cgacgtgtgg tgagctctca ctggggcgtc cctctaagat ctgtccactc ctggtttagg 1020
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ntt 1083

<210> 115
<211> 913
<212> DNA
<213> Rattus norvegicus

<400> 115
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taanataggt ggggnccnaa aancttgatt ttccctttc cctttgantg nntaaagttg 120
cnaanttccc tttggacgcc ntttacaaga ttagccngtg tgtaaccttt gggcccttta 180

acaggattnc ttggccntnt gaaacacgta tttatgtcag gnttntaccg tngcaaantt 240
ngttttgagc agcaacgaaa tcactttatg gttggaggtc accacaactt gaggatgtat 300
taatccgcag tattagagag tcgagaacca ntatcttaga ggatcggtag actgatgttt 360
cccntttngc ttggagttgn cttnccacta gaggcaacag catcagtatt gttccccagt 420
ccccctcaca ttgattcgaa ctttaaggac actgatctct ggcttggtag agggttcagc 480
acacatacca gagttacgag tcacgtgcca gaaggcaaac tgaacacgga attagaggga 540
actcgatgtc tccggcttgc actggtcttn tcttgcacta gaatcnttca tcntgctccc 600
agtccgggac gtccaggcaa caagggcgtg gaaagtgagg gggctgggag gtgtgtttgc 660
cttgcctcag gcgctgggtg gggttggggc gtgccagcac tccctgggcg ggcctcaccg 720
atgctggcca ctataaggcc agccagactg cgacacagtc catcccctcg ccactctttt 780
ggcgcttcat tgtcgacgtg tggtgagctc tcactggggc gtccctctaa gatctgtcca 840
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gctaaatgag atc 913

<210> 116
<211> 1123
<212> DNA
<213> Rattus norvegicus

<400> 116
acgcnatntt ggtggaattt ggggggtaaa aattttnaac gaattaggna ncttagggna 60
cnaaatccga aatggggaat ngggntaaat ttcgaaccnt ttnggaggnn ntaaatntaa 120
aaatgaggnt aattggnttn gaaangcnta tcaggcattc caaattntta aatttccctt 180
ggccagagat tggggaaaat tttncccgga ntccagnttt aggttnnttg gaaaaacggn 240
gccccaggga ttgttgcacc nttcccaatn aaggnggttt tccntccaan gcctttnggg 300
gnaaacccag gggggnttn aggggcccaa ttcaggaaaa ggggaccgga ntcgggtccc 360
ggaaggnttc ccggnggga atcaacccgg ttcccntccg gaggccgggg gggaccttta 420
ggtttcccct tgcaggggta anatcccctt tttcaacccg gggggtttgc ggggnacgcc 480
cctttgccct ttcccttccc ttgccnggcc cgttttgccc aattnggccg gtcctaactt 540
gttggcgcaa gggacttttg gcagccccgg ccggtttggc ggttggactc caagggggta 600
acagggccaa accntttggt tgaaanaagt taacttgcgc ccccagtcan gcgtcagtgg 660
gnangtgacc ccgcntttag gagtttgccc cngccnttag gccttgcccc cagaggtcgc 720
cccacntact agagtgtcgc ttggcgcgat gacgtangan gacgcaggcg cagtgagtag 780
gcgacgttgg gacggccctt ggttgtgtcg gggcggaac tntgntggct ttgagcgcct 840
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aaacagggat cctccagtcg tgtggaccga cccgagtccc gcaccctttt taaggcctgt 960
gttgcggatc cgcgcggcca tcacgcattg catcacggtt ttactgtgtg ggaaacgtag 1020
ccgtccatac ctgggtgtag tcagggacct ttatggtggc tgtcacgcag gcgatttgnc 1080
aattgaaaga ctttnncctg taggnanggg nagctaaaaa gat 1123

<210> 117
<211> 1116
<212> DNA
<213> Rattus norvegicus

<400> 117
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cccccttgna anttttcccc gtaaataagg naatgntgna nttgtattta ncttgcccaa 120
aaaaaacnnt gttcttnaat gcaaggtant tgggggttat tattntgaaa ggcaactaat 180
tnttaatggt ggattnaaca attttgaagn ggattaaana aaanaaatna ttgntttcca 240
ttggnggtgt gggnttaaaa cccttggtnn ccagggttcc antgggttca ggccctttga 300
gngggntccc cnttccccgg gaatnggntt gaaccggaaa ttgaacattt tgcacccttt 360
tccggnggcc cttaaggatt gcagcnccag ttgcggggaa ggggtaattc cttgcccncc 420
gtggaagggg tttcagnttc cttcccaacc cccccccggc cgggagtccg gnggggcggt 480
ttntttcacc ttaagggcgg gcgtggantt aaattaagcg ccggggnggg ntcccaagcc 540
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cggttntccn nccggccaac cgggncccgt ggttgntggg ttaggccagt gcaccnggag 660
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aacacagtgc tgtactagta cacacacaca cacacacaca cacacacacg ttacacatgc 900
tgacacaaac atgaaaatgc agtcaacggc aggcagagat ggatggatgc acattgctgt 960
ggaatggtac actttgcacc tcacactctt ccagagggac agtccataca acactcagct 1020
tcgcttccca ctataggctt cacatgacca gctcttcagc gtcggaaagg acngtactga 1080

aagacttnac ctgtaggnng gncagctaaa aagatc 1116

<210> 118
<211> 900
<212> DNA
<213> Rattus norvegicus

<400> 118
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tgtgggggnt antntgtatc ccctnnnctc nctcgaganc ccnnntctcg anattttggn 120
gaccngggc cggggcccag anactcncca ccccatatgg ngaccctnta taagtgtcnn 180
ccagggnntg ttttgggnaa aatatancnn anagnggtgt ntntnanatc tcgggggtg 240
acagacccnn attttttttt ataaagaccc ggggcatntt ctcngccccn tctcctcngc 300
tacangnnac ccacacacag tgtgtctcct ctcagccccc tggcacactt tntntngant 360
cngngggat atgagattcn cnagactggg nccgcnntan tanncncccc cntgtctcct 420
ctcatagtgt ngtgtccccc cctcacccnn tnttgnggtn ccctacaccc acacaatnta 480
gactctnccc nccntcngct ntgngacnca canctgnaaa tcccgnnncn caaaaagggc 540
tgtnctcctc tctnttacng ggnggtcncc cncnnnngac tctnaaangt ccctcncaaa 600
agggacnctt ttctatacac ncttantttn cctcctttgt ntngcaaaaa annancctgt 660
gttnccccc nctttatnat ntttnttttn ttccccaaac taancttta ggnntnanct 720
tccgggccc caaccccaaa atcccantnt tcttttntnt tggttggggt gtcaaaattc 780
ctnccctaa anttttgaac cccctttaat tccccccccc ggntnaaggc ccnacttccc 840
tnggntnttt tcnctaaaaa attttttgtn gccctccctg ggaaatcccc ggtattcctc 900

<210> 119
<211> 498
<212> DNA
<213> Rattus norvegicus

<400> 119
atgttgtgtg gaattgtgag cggataacaa tttcacacag aattcagaag gatctcagaa 60
attgaaagca tgtgcaaaga taaagatttg ggtagtagt agtggtcaaa agggacaagg 120
taataatggt aatatgcttt tgtgtatgtg ttcttttaga gttatgttaa aatctagaga 180
agcaaagtcg attctcatag atgcttttag tctttggacc ctgactagag acagtttaca 240
ccctagacaa gagagagaat ggggttgagt aaaacagtcc tcccgaactc tccacagatg 300
ctttggcaaa agaaggaaat gagcttaaac tttttggagc tctcctggga acagaaggag 360
gtgggagacg tcttgcctcc ttgctgctcc tattggagaa gtgcttattt ctggttctgg 420
gttttttagg taggntgtct gggtcccttt ggtntgaaag accttacctg taggtttggn 480
cgntngaaaa gatcntgg 498

<210> 120
<211> 380
<212> DNA
<213> Rattus norvegicus

<400> 120
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nccgggaacn tgnaaacatt gaccaanctt gttttaatta ccggtttggg gnaaaagggg 120
caaccccaaa ggggaaggga anggaangga aaatnaattn cctttnnaaa aaggagnaaa 180
tncgggtang gaaaattccg gtgnggggtt ttcaaaggtc cccccccgnn ggnntaaaaa 240
attgaagttn antcnngggg gggaacccaa nagaatataa anaaaccggg gtttccccn 300
gggagttcct tggggggtttn ccggttcgac ccgncgntta ccggaaacct ntcncctttt 360
tcccttgggg naggggggg 380

<210> 121
<211> 998
<212> DNA
<213> Rattus norvegicus

<400> 121
acatgtacac aactgggtcc cagccaagtc aggttccagc tgccagcaga ggcctggagc 60
tagcttcgcg tgcactacca ccctgcccaa cctggcactg tgcccattga cttcgggggg 120
ccgggggcag gaggtaccca cctccccacc ctcctcttcc ctcctctcag gagcttatct 180
atcggtgagc agcaagtagg aaaaggtaag ctgagaaaga gcacttggct ggctacagga 240

cctcagcctg aggtgtgaaa caggagactg ggcactgggg aaacagcagc actggctggg 300
ccaaagggga gggaggaagg caatgaatgg gcaagcctgt gccttacaga aacagactcc 360
cttgggctgg gtgctggaat cctaacccct cagtgatggg ggaactctgc tccagtgagc 420
tgaagtatac atgtggggaa ttggggggtg gggtaggggg aaggcaatcc aaaggtcact 480
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ctggtttctg gaaagaaggg agttaatcag caaacaattt aagaaaggta taactgtcta 600
cccctgcaga ggatcatggg ttncctctct annettctga gccgtggatc tcagccaaaa 660
acaaaaacca aaacaaagaa acaaacgcct atttaaaagg gggttggagt tgggcagggg 720
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cnccagagag gaaaacaacc gcctagttaa taagcagagt tgggctgttg gcaaaccgtc 900
attccagatc tgaggnaagt tggatggttc gggtgtctat gttnacntaa gacctgtttt 960
acaagctnnt atgggcaagg gctttggttc nagnaagg 998

<210> 122
<211> 970
<212> DNA
<213> Rattus norvegicus

<400> 122
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tgggttttta acggcttttt ttanaaggcc nagataccct tttnatggcc tttattccct 120
tccgttttnt tcccccccctt caatttggaa gtttggtttg ccgaanttta agttnttgtc 180
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aaggntnttn ttgaacccgt aatngcggnt ttccggttaa ccnagggttt gttcctnngc 300
cgnttcctcc aatttttgga ntttcccagn tnggggtccn ttntcttgtt nacngttcca 360
aacntaattg acanttaatt tttcctgtgt aanttgtccc cgganattnt gggntcttgg 420
ngcagggcct tttttcattg gaagcaaccc cntaaatttt taccaggctt gattgtttag 480
gaagtaatcc ttgcttngaa nccccacttn ttntttccaa ggntggaaac caggattttg 540
gaactgcaga ggcttcaggg tctgggaagc ggagcangca aagantggag tgcactgtcc 600
ttttgcaata tggggtttgc ttgcttgctg gctcntntcn tgctntntca gatggtgact 660
gaggctactt cagcaggact aggaataatc atgtccaggt ggntgccctt ccgagcagaa 720
agggacagac gtggggcgat gaagttgcta tcgttttttt ttttttctgc acagactgca 780
aagtgtgcag agggagggag gctgtgcaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaac 840
cgaggacgca gaagttagac tgctgaccca tttggtgcat gtgtgcccat ggagggaggg 900
gaccttctca aaagggttca cgcagcaagc attgaaagnt tccacntgta gngtcgcaag 960
caactgagat 970

<210> 123
<211> 884
<212> DNA
<213> Rattus norvegicus

<400> 123
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agaagcaatt tagtgtcctn tgtcctctga cctccacaag tgctgtggca tggggacaca 120
ggactgtaca cacacacaca cacacacaca cacacacaca cacacacgca cgcacacaca 180
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ggctctttca gaaccaggag ggcatcgccc ctccagccag actctccagc tttcttcccc 360
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tcccagggct tccaggantt aggggtatac caggccccann acattgggna aacgtgtgtg 780
tnaannnttt cntntnaaac cnccnnggtt gacnactngn nntccntttn aanggnccca 840
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<210> 124
<211> 855
<212> DNA
<213> Rattus norvegicus

<400> 124
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tnacgagggn attnggggtt anagttttgg agtgggccaa nangaacatg gaggaatatt 180
tgttttggtt tgngaaccat accttggaaa gattgtattt ttatccgcca acaaccacng 240
tggtagggtg tttttttgtt tgcagcagca gataagggca gaaaaaagat ntcagagatc 300
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cacacagcaa ggagaggagc caatatagag gggaaaaaaa aagaagggga aagcagttag 420
tttaaaaagt tgagagaaca aagtatgttt tgnttggatg ggcaaccaaa gaagcntgcc 480
aggaatggtc ggtaaaaggt gtaagagtca tgaaagtntt ctgtccaacc gttaccggaa 540
acatgcaagg aatttcttag actggccagg attggattgt gggaaaggtn tnttcaagcn 600
tccccttggc ttttatggca agaaaatagt gcggactata gagagcgtcg ttctcaaagc 660
tttccccaat agcagaaaag cattgtccta aattccctaa aaggcaccgt gaaataaata 720
ttacgggaca cgatggcaca agaaggagct ttcaactctg ccaccagaac agttatactt 780
catagtaacc atgttgccct gttcaatgac aaggcacgct ctccagcaga aagggaaaag 840
gagctgagtt cgcac 855

<210> 125
<211> 1059
<212> DNA
<213> Rattus norvegicus

<400> 125
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ntttnaaccc caaaaccatg nnttgncctt tcccctnacc ngtnatagtg nttgnantgt 120
aacccaacaa tcaacggnta tttgttcagg ganttnttgg taccaggcnn ttggttttga 180
naanacggta ggtccgggaa gcnttgacgg taagcccngg gganaagggc caacggngat 240
cccaaattag gagcttgacg cattgttttc ntttgcntgg aatgncattc ttctcttctc 300
cntttatcta gaaaacgntt actcatgctt caaanccacn gttgacttcc ccagcattgn 360
ttcncntagc tccttctttg aaacaactga ttgggaaatc aggaggatan gaaaagcttt 420
aacaagagct ttcaggggct ttcggagaga actcattctt gtaggacgca ggccatgcaa 480
gcatcaggct ctgccttctg gaccccagta tacagacata tgcacaactg cagtggttca 540
tacttgtaat cccagtgtta ggaagactta gacttggagc ttgctggtca gactggtaag 600
cccagttcag tgagaccctg acttaaaaat gaagttggaa agaaatttgg aaagataatc 660
tggtattcat ctctgggctc tatttgcaca ggcacacaca caaatatacc aatataacat 720
acacagaaag agaaggggag ggaggaagag agggagggcg gtagagaact tgtgaatgtc 780
ttttgatagg tttttttttta agttattgga ttaaaccatc agcagtgtca cattggttaa 840
gttaaaaata ataaaatgaa gcaacttatc tttgctgaaa ttcattactc attatgagag 900
tttgataaaa aaaaagagga gtctcccaca gttttcctgt ctcatctttt actccagggg 960
acggtcacac tattcagtaa gatacctagg ctatctggct cactggactn ggcgtgaaag 1020
actnnacctg taggtttgng cgctgaaaag atcttnaac 1059

<210> 126
<211> 1042
<212> DNA
<213> Rattus norvegicus

<400> 126
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tagagaaata ggcagcacag gcctaacagc ccatantgtg tgctattcta tcaatagtgc 960

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<210> 127
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<212> DNA
<213> Rattus norvegicus

<400> 127

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